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DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

FOOD AND DRUG ADMINISTRATION

ORTHOPAEDICS AND REHABILITATION DEVICES

ADVISORY PANEL MEETING

OPEN SESSION

Tuesday, June 10, 1997

9:00 a.m.

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2 Montgomery Village Avenue
Gaithersburg, Maryland

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P A R T I C I P A N T S

Voting Members

Barbara D. Boyan, Ph.D., Chairperson

Marcus P. Besser, Ph.D.

A. Seth Greenwald, D. Phil.

David L. Nelson, M.D.

Keith Markolf, Ph.D.

Roger M. Nelson, Ph.D.

Leela Rangaswamy, M.D.

Sally A. Rudicel, M.D.

Harry B. Skinner, M.D.

Non-Voting Members

Doris Holeman, Ph.D., Consumer Representative

Raymond Silkaitis, Ph.D., Industry Representative

Also Present

Dr. C. Witten, Div. General and Restorative Devices

Jodi Nashman, Executive Secretary

CONTENTS

P R O C E E D I N G S

OPEN SESSION

MS. NASHMAN: Good morning everybody. We are ready to continue this meeting of the Orthopaedics and Rehabilitation Devices Panel. As a quick reminder, I would just like to remind the members of the Panel that what you heard during the closed session is to remain there; it is not to come forth into the open session.

Again, my name is Jodi Nashman. I am the Executive Secretary for this Panel, a biomedical engineer and a reviewer within the Orthopaedics Branch.

I would like to remind everybody that you are requested to sign in on the attendance sheets which are available on the tables by the doors. You may also pick up an agenda and information about today's meeting, and also how to request transcripts, by the doors.

For the benefit of those who were not present at yesterday's session, and I believe that will be the majority of you, I am going to reread two statements that are required to be read into the record. That will be the deputization of temporary voters and also a conflict of interest statement.

Pursuant to the authority granted under the authority granted under the Medical Devices Advisory

Committee Charter, dated October 27, 1990, and as amended April 20, 1995, I appoint the following people as voting members of the Orthopaedic and Rehabilitation Devices Panel for the duration of the Panel meeting today, June 10: Marcus B. Besser, A. Seth Greenwald, David L. Nelson, Roger M. Nelson, Sally A. Rudicel and Harry B. Skinner.

For the record, these people are special government employees and are either a consultant to this Panel or a consultant or voting member of another panel under the medical devices advisory committee. They have undergone the customary conflict of interest review and they have reviewed the material to be considered at this meeting.

Also, because the position of panel chairperson for the Orthopaedic and Rehabilitation Devices Panel is currently vacant, I appoint Barbara D. Boyan to act as temporary chairman for the duration of the Orthopaedic and Rehabilitation Devices Panel today. For the record. Dr. Boyan is a special government employee and is a voting member of the Orthopaedic and Rehabilitation Devices Panel. Dr. Boyan has undergone the customary conflict of interest review and she has reviewed the material to be considered at this meeting. This is signed D. Bruce Burlington, M.D., Director, Center for Devices and Radiological Health, and is dated 5/28/97.

I have the conflict of interest st atement also to be repeated because yesterday I accidentally omitted a page. The following announcement addresses conflict of interest issues associated with this meeting, and is made a part of the record to preclude even the appearance of an impropriety. To determine if any conflict existed, the Agency reviewed the submitted agenda and all financial interests reported by the committee participants. The conflict of interest statute prohibits special government employees from participating in matters that could affect their or their employers' financial interests. However, the Agency has determined that participation of certain members and consultants, the need for whose service outweighs the potential conflict of interest involved, is in the best interest of the government.

Waivers have been granted for Dr. David Nelson and Dr. Harry Skinner for their interest in firms which could potentially be affected by the Panel's decisions. The waivers permit these individuals to participate in all matters before the Panel. Copies of these waivers may be obtained from the Agency's Freedom of Information Office, Room 12A-15 of the Parklawn Building.

We would like to note for the record that the Agency took into consideration other matters regarding Drs.

Boyan and Seth Greenwald. Dr. Boyan and Dr. Greenwald reported interest in firms in matters not related to the agenda before the Panel. Since these matters aren't related to the specific issues of this meeting, the Agency has determined that they may participate fully in today's discussion.

In the event that the discussions involve any other products or firms not already on the agenda for which the FDA participant has a financial interest, the participant should excuse themselves from such involvement and their participation will be noted for the record.

With respect to all other participants, we ask in the interest of fairness that all persons making statements or presentations disclose any current or previous financial involvement with any firm whose products they may wish to comment upon.

At this time, I would like to introduce our Panel members before turning the meeting over to Dr. Boyan. For my own ease, I am just going to read everybody who is participating in alphabetical order: Dr. Boyan, who does orthopaedic research at the University of Texas Health Center, will be serving as the chairperson for this meeting. Dr. Marcus Besser, a biochemist at Thomas Jefferson University, is a consultant deputized to vote at this

meeting. Dr. Seth Greenwald, an orthopaedic biomechanics specialist at the Orthopaedic Research Laboratory at Mt. Sinai Medical Center, is a consultant deputized to vote at this meeting. Dr. Doris Holeman, at Albany State College, is the consumer representative for this meeting. She is a non-voting member. Dr. Keith Markolf, a biomechanist at the Biomechanics Research Center in the University of California at Los angeles, is a voting member of the Panel. Dr. David Nelson is an orthopaedic surgeon, a consultant deputized to vote at this meeting, who also is not to be confused with Dr. Roger Nelson, a physical therapist at Thomas Jefferson University, who is a consultant deputized to vote at this meeting. Dr. Leela Rangaswamy, an orthopaedic surgeon and deputy editor of the Journal of Bone and Joints Surgery, is a voting member of this Panel. Dr. Sally Rudicel, an orthopaedic surgeon at Tufts University, is a consultant deputized to vote at this meeting. Dr. Raymond Silkaitis, the VP of medical and regulatory affairs at Gliatech, is the industry representative to this meeting who is non-voting member at this meeting. Lastly, Dr. Harry Skinner, an orthopaedic surgeon at the University of California, Irvine, is a consultant deputized to vote at this meeting. Lastly, I would like to introduce Dr. Celia Witten, sitting at the far

corner of the table, who is the Division Director of the Division of General and Restorative Devices.

At this time, I would like to turn the meeting over to Dr. Boyan.

DR. BOYAN: Thank you, Ms. Nashman. We would now like to continue the meeting with a discussion of the second PMA being presented before the Panel, J&J Professional, Inc., Poly-Dial Constrained Liner.

I would like to remind public observers at this time that while this portion of the meeting is open to public observation, public attendees may not participate, except at the request of the Panel.

We are now ready to begin with the sponsor's presentation. I would like to ask that each speaker state his or her name and affiliation to the firm before beginning their presentation. Just as a comment, during the presentation I think we have one of the devices which will be moving its way around the Panel for us to review, and here it is. So go ahead, and keep it and just pass it around. Welcome.

Presentation by Sally Maher, Esq.

MS. MAHER: Thank you. My name is Sally Maher, and I am the Director of Regulatory Affairs for Johnson & Johnson Professional, Inc.

It is my pleasure to be here this morning to present the data demonstrating safety and efficacy of the S-ROM Constrained Liner, and supporting approval of this premarket application.

I would right now like to show you the agenda that we intend to go through, and would ask that you hold any questions until our presentation is completed. Thank you very much.

These are the indications for use that the FDA has actually suggested that we use for our device. It is slightly different than the indications for use that have been in our insert for the last seven -- ten years, since 1987, but only slightly different, and we agree that this would be a perfectly adequate indication for use for this constrained liner, and is supported by the evidence that we will be presenting today.

I know that Dr. Boyan said that she was sending around a sample of our product. I have a couple of other toys to show around. I am doing it in support or to show what the definitions of constrained really mean.

This is a definition of constrained that is found in the Federal Register, Code of Federal Regulations at 888.6a, and this is a Sivash hip, and I will be passing it around in a second. The Sivash here was launched in 1972,

and it was put together at the factory and, as you can see, it doesn't come apart. We tried to get it apart.

The definition, if you look at it, states that this device, constrained device, will prevent dislocation, and this is one of the types of products that the Panel and the FDA was considering when they came up with this definition.

This is a definition for the semi-constrained device, and this is our S-ROM semi-constrained device. As you can see, it is totally modular. It limits translation but it clearly doesn't keep dislocation at all.

Now, this, what you have in front of you also and I will be passing around -- yours comes apart, ours is put together the way it should be, and this is one of the locking screws that we use, included for safety, as you can see. It is the S-ROM constrained liner, which is derived from the S-ROM semi-constrained. The major difference between the two, and our engineering group will go into this in a little more detail than I can, is that the equator -- the liner goes past the equator of the hip head and has a metal reinforcing ring to limit the ability of it to dislocate. So it won't come apart as this one can.

This product clearly has a need. It has a niche market for the people who have chronic dislocations. It is

used in special situations when this one clearly just won't do. But it is also very different from what was on the market in '72 when those definitions of being constrained (sic).

The constrained liner, which you all have been looking at, was put on the market in 1987 in the United States. We launched it in 1995 in Europe and Japan, and there were other countries it was sold in in between those years but, in essence, over the last ten years we have sold 6000 units. The product is well established. It has been on the market for a long time. We have no evidence that there have been any problems with this product, and the data that we provided in our application clearly supports the safety and efficacy of this device. It is for a limited patient population, as I said, and for those patients there frequently will be no other alternative.

However, in addition to the indications for use that the FDA has presented, we believe that this labeling information needs to go in the insert as well, and that is because of the type of liner it is and the reinforcing ring, and the fact that the liner goes past the equator of the head, positioning and accurate aligning is even more crucial to prevent impingement and, therefore, dislocation.

Now I would like to turn it over to John Ferros. Mr. Ferros will be presenting the regulatory history of this device, how it came from the Sivash, and the complaints and MDR history we have in our files. Thank you very much for your time.

Presentation by Mr. John Ferros

MR. FERROS: Good morning. As Ms. Maher stated, my name is John Ferros. I am the senior regulatory affairs specialist with Johnson & Johnson Professional, Inc.

As she also said, I am going to be talking today about the regulatory history of the S-ROM Poly-Dial. What I am going to do, I am going to go over a chronological overview of where we have been in the past and where we are today, and also I will be talking somewhat about the complaints and the MDRs that we have seen with this product.

The reason I am going through a chronological overview is just to give you a frame of reference of the entire history of the device and its evolution. One thing I wanted to stress, I know Mr. Dillard spoke about this yesterday briefly, but we want to stress that it is important to understand that this PMA that we are presenting today is different from most PMAs that you have seen in the past, and that is, we are not here to present a new device

with new technologies. This is really in response to a regulatory requirement, that is, FDA's calling of PMAs.

With that in mind, I want to go directly over here to this overhead and talk about the chronological history of the device. In 1972, the first Sivash hip was launched here in the United States. This is what Ms. Maher was talking about, the fully constrained device. 1976, the Medical Device Amendments, of course, as we all know. 1982, the Orthopaedics Classification Panel proposes a classification for a number of orthopaedic devices, one of which is the constrained hip and, at that time, the panel proposed that the constrained hip to be in Class III.

Now, at this time, of course, the recommendation was to classify prostheses for hips, such as the Sivash, which was the known hip at that time and the state-of-the-art.

Moving on to 1987, Joint Medical Products submits a 510(k). Joint Medical Products is no longer a corporation. It was acquired wholly by Johnson & Johnson Professional, Inc. in 1995. So, therefore, this corporation no longer exists. However, the 510(k) was submitted in '87. At that time, when the submission was sent in for this device, Joint Medical Products stated that they believed that this product was a Class II device. And the reason they stated that was

because of the similarity of the Poly-Dial semi-constrained device which had already been on the market. Substantial equivalence was granted later on in that year.

Moving on again to yet again in 1987, a final rule of classification was brought forward. During that final rule -- included in a number of products was, of course, again the constrained hip, and that was finalized as a Class III device.

In 1995 FDA proposes calling for PMAs and finally a final rule for that calling of PMAs came into effect in 1996.

When FDA published that final rule, the final rule required a PMA to be filed on or before December 26, which Johnson & Johnson Professional did. We submitted on that date and here we are brought to this point, right here, in this Panel meeting.

So again, the reason that we are here is because this PMA was submitted not because of new technology but, rather, because of a statutory requirement.

I want to move on to complaints now to give you an overview of what our complaints and MDRs are like. This is a breakout of the complaints that we have seen -- the complaints that we have received and the MDR reports. As you

can see, the first few are self-explanatory -- alleged contamination and so forth.

I would like to jump down to dislocation, which is number five. As you can see, we have received 16 complaints for dislocation. Of those 16 complaints, those were all reported as MDRs. That 16 plus 4 needs a little explanation right there. The 16 plus 4 -- the 16 underneath the MDRs goes along with the dislocations that we have had; the 4, with the asterisk that you see below, goes with the 22 dislocations that were reported from clinical literature.

When we were putting together this PMA we, of course, looked through the clinical literature and in there we discovered that there were 22 dislocations. Those were reported from 4 distinct clinical papers and they were reported as MDRs.

If you look down to the rate of complaints and MDRs, .68 percent is the complaint rate that we have if you take into consideration over 6000 sales that we have had of this product, which is actually a conservative figure which would bring that number actually even lower, and also the .72 percent MDR rate is also using 6000 sales, which is again a conservative figure. That .72 percent, as you can see, includes the 22 clinical literature.

Lastly, as I conclude I want you all to take into account that that is quite a low complaint rate and MDR rate, and we feel that with this low rate, along with the clinical history of this device, this is good evidence to show and support the safety and efficacy of our device.

This concludes my portion. I want to introduce now Mr. Doug Noiles. Mr. Noiles is the engineer who is responsible for designing this product and its evolution from the 1972 Sivash hip. Mr. Noiles?

Presentation by Mr. Douglas Noiles

MR. NOILES: Thank you, John. Well, I am Douglas Noiles. I am a professional mechanical engineer. I am an inventor; I am a consultant; and in the vernacular of the younger generation, I am "history."

(Laughter)

Half -- more than half of my 50-year career has been devoted to the medical device industry. I was vice president for engineering for United States Surgical Corporation through the whole decade of the 1970s. I was founder and vice president for engineering and product development for Joint Medical Products Corporation from its inception, in 1982, until 1995 when the company was acquired by Johnson & Johnson.

Slide please. Simply, there are patients for whom a constrained total hip replacement is indicated. If one takes a very conservative view and says we will make all primary or first hip replacements as semi-constrained, one must also expect that there will be chronic dislocators.

Now, without a backup the prognosis for some of these patients is rather miserable. There are several alternatives to a constrained socket -- alternatives. None are really universally applicable. A bipolar hip has problems. Link has developed a crutch type prosthesis that runs directly on the pelvis without acetabulum. Fusion is not done much any more. Flail hip or a girdle stone is very unsatisfactory.

So it is very important to the surgeon that he have a backup; that it be interchangeable in situ, and this means that it is interchangeable without disruption into the bone interface with the prosthesis.

Slide please. Now, we seek authorization to continue selling a product with more than a quarter century history of development, manufacture and use in the United States. When the Sivash prosthesis was originally redesigned for sale in the U.S. two versions were made, a metal liner and a polyethylene liner. They were dimensionally identical. They were assembled at the factory. They were sterilized as

a unit and installed as a unit, removed as a unit. They didn't come apart.

That is only partly true. The second entry, the polyethylene did come apart in patients. It did not constrain well enough. So in 1974 there was a design modification to add a reinforcing ring to the polyethylene insert.

In 1984 was the introduction of the S-ROM modular, orientable, asymmetric insert, which was a pioneer and really a remarkable development -- very simple but remarkable development in hip prosthesis design.

The first four items are four different levels of constraint. And I look at the first one, the metal liner, in terms of Eskimo numbers. I understand or there is a story that Eskimos count from 1 to 20 and any larger number is "a whole lot."

(Laughter)

That first liner, in terms of resistance to dislocation, is "a whole lot." It was never tested until recently but it exceeds a ton and a half and nobody really knows what it fails at.

The second entry, the polyethylene original version, would pull out at somewhere between 100 and 200 lbs. It wasn't sufficient. The reinforcing ring, added in

'74, increased the torque's direct pull-out strength to somewhere between 250-300 lbs., and has proved to be satisfactory.

So when Joint Medical was founded surgeons who had used the Sivash prosthesis and saw some advantages in it continued to encourage Joint Medical and used its products, and shortly after 1984 they were requesting that we add a constrained prosthesis to the line. So we did this, and it was introduced in 1987.

Now, what we did was take the design of the ball-to-insert interface from 1974 and incorporate it into the modular construction without change -- mechanically no change. This is an interface that is unchanged since 1974, 23 years. At the bearing or insert to the cup interface we used the successful 1984 S-ROM Poly-Dial modular insert design. So the outside of the bearing has a design unchanged since 1984, 13 years.

In addition, independent lab tests have shown that the S-ROM design provides a good degree of security of the bearing in the cup and a good amount of mechanical support for the polyethylene.

Now, in the hip prosthesis the alignment and range of motion are related. And I think one can say that the range of motion measured in the laboratory is not exactly

the range of motion in the patient. In the laboratory we measure direct excursion back and forth. The patient's flexure includes rotation and there is evidence that the constrained S-ROM prosthesis has range of motion which is totally adequate for the patient where its use is indicated.

Now further, the 1983 Joint Medical Products' introduction of the invention of the skewed orientable liner, and I say 1983 because we showed it at the cabinet meeting that year when the application was filed. This is a very important development, particularly with respect to this constrained liner, because alignment is critical and its marginal orientable construction permits the surgeon to achieve a higher degree of appropriateness in alignment. The patient requires a certain range of motion; the prosthesis provides a certain range of motion. It is important that these two be brought together, that the prosthesis allows the patient to move where he needs to move.

Failure -- we see in retrieved specimens just about universally that dislocation is due to impingement. The testing of direct pull-out -- we don't see the prosthesis failing that way. You would have to get the patient in a certain position and pull on it, and pull on it and it just doesn't happen that you have abduction to 45 degrees, and anteversion when somebody pulls and pulls on

the leg. But when there is impingement, there is a very great mechanical advantage by leverage, and it doesn't take an awful lot -- the torque value for failure by impingement and leverage is, I believe, about 150 pound-inches. It is a fairly big number but when one thinks of the force at the knee on the hip, we are only talking about 10 or 15 lbs. to dislocate the prosthesis. So it is not constrained in the sense of the original prosthesis.

I just thought this morning to describe this whole design is something like a Mercedes with crumples on it, so that when you have a crash and if it is a little one you bend the bumper and if it gets bigger you crumple up the front of the hood, and so on, and it is designed to protect the passenger. So this device has a design sequence that if there is a dislocation, the sequence is the ball comes out of the socket. The next higher strength is the joining of the socket to the cup, and the next higher strength is the cup to the bone. We have not had a history of disruptions of the prosthesis from the bone, which would be a catastrophe from the surgical point of view.

One published report of disruption of the cup from the bone, and this was the result of trauma -- I don't know of any other. So alignment is critical to preventing impingement, and if there is a failure by impingement there

is a high likelihood that you can't reduce this as a closed reduction. It would be an open reduction to replace a dislocated constrained socket. Now, that sounds major but it is not major to an orthopaedic surgeon, and the damage is only to the insert whether around the ball or in the cup, and it is an easy mechanical matter to replace.

Now, patient instructions -- instructions to the patient postoperatively are very important. This is not a cure for misalignment and no one should interpret it so.

That is the end of my talk and I would like to introduce Jorge Ochoa, the manager of hip, arm, knee at Johnson & Johnson Profession, Inc.

Presentation by Jorge Ochoa

MR. OCHOA: Thank you, Mr. Noiles. It is a pleasure to be here, ladies and gentlemen, and the Panel, and it is my charge to present to you and summarize the technical data that was already put together in the PMA packet for you, and just go through some of the formalities and some of the technical details to backup some of the clinical data that we have.

So without further ado, the first thing I want to do is, aside from the fact that some of these samples have been going around and they are labeled, and they are very informative, and it is a very didactic way of starting the

presentation, I want to give you some descriptions of the device components, some description of their function, their materials, how we clean, sterilize, just to bring us up to speed on the fact that these are state-of-the-art materials.

The subject device itself is an ultra-high molecular weight polyethylene liner, with a titanium alloy reinforcing ring around the opening of the liner. And that liner and ring do not stand alone. They are used with a system, a modular system of components which include an acetabular shell or various types of acetabular shells. Then there are peripheral dome screws which are used as adjunct fixation for the cup in order to secure the cup to the bone on the periphery of the cup and on the dome and, of course they need to be used with a femoral head and femoral components already out there, in order to complete the joint connection across the hip joint.

I just briefly want to go through the indications because this is something that as mechanical designers and bioengineers we need to keep in the front of our mind, not in the back of our mind, and when we design, test and evaluate these types of devices we are always concerned with the indications and, as the FDA has stated and as we have currently put in our package insert, there is a need for the prosthesis such as the constrained Poly-Dial liner,

especially for patients that have a high risk of dislocation either for primary or revision surgeries. These patients that have a high risk for dislocation, there are many causative factors. They can be biomechnical; they can be pathological; and sometimes there is instability in the hip that is not immediately evident but becomes evident intraoperatively.

So as Mr. Noiles said, it is important that we have not only a gamut and a continuum of constraint available, but the fact that this constraint can be evidenced and implemented by the modularity of the device.

A very busy slide just to point out that the liner itself has many sizes available specifically to address what Mr. Noiles said, the fact that we have a dialable modular insert that has neutral and augmented face angles that are available to the surgeon in the operating theater, and also the fact that it can accommodate the different sizes of femoral heads that are standard out there, as well as some on a custom basis.

What is important here is just to point out that these liners are modular. They can be used in various shells. They do address the continuum of constraint and they are used with cup systems that are already sold by Johnson & Johnson Professional.

Here are some product images just to give an idea of the different components. The bottom square is a sample of a couple of the cups with which the liners can be used. The top right is an assembled device with some of the peripheral screws that are used for fixation. In our package insert there are some notes that we make regarding the performance and use of this specific device which I will address.

There is also a schematic of the design itself there with its representative dimensions, just to show that the opening for the femoral head does come around. The equator does provide a snap fit, which is relieved by some slots, and then the reinforcing ring is put in intraoperatively. On the left is just to show that it is a modular device and can be interchanged.

In the packet insert we do speak about some of the issues. For example, this device should not be used with ceramic heads. We ask the surgeon to put the cups when used with the constrained liner because of the slight difference in biomechanical loading. When not using a constrained liner, then possible impingement and different biomechanics, to use the screws, to actually screw the cup and fix the cup into the acetabular bone to gain that staircase sequence of design as far as how this would fail or dissociate.

Also we speak to the use of heads of different diameters. The smaller the diameter head, the less range of motion, for obvious reasons because you have less of a diameter to work with. Also we address the fact that since this is already a relatively small motion compared to other semi-constrained hips, not unusually low so as to prevent normal function but heads with skirts, especially the smaller heads with skirts are not to be used or to be used cautiously because it could reduce the range of motion below where an orthopaedic surgeon would like to help the patient out with.

Some very standard comments about the materials. The line itself is ultra-high molecular weight polyethylene. Complying with ASTM standard F-648 and the titanium components are either ASTM F-136, which is the titanium-6 aluminum 4 grenadium Eli alloy, which would be the substrate of the cups and the reinforcing ring. In the case where the cups have a porous coating, the powder is commercially pure titanium and it does, like I said, comply with ASTM F-67.

These materials are widely used in the industry. They are used by us in all of our hip and knee devices at one point or another. They have been used for a long time. Their biocompatible use is demonstrated so it is nothing out of the ordinary at all. The design is little out of the

ordinary because it is the constrained versus semi-constrained, and that is where the difference comes up, not in the materials.

These devices are packaged, clean-packaged and sterilized by standard methods as used with all of our other orthopaedic implants, and these sterilization processes are validated and documented, and the package integrity for the type of packaging we use has been validated to a minimum of five years and these tests are undergoing, so we keep collecting these data. So here there is nothing out of the ordinary; very standard materials, packaging sterilization that we use with all other orthopaedic implants.

As Mr. Noiles said, there are a couple of interfaces that we need to speak to, the first one being the interface between the head or femoral component and liner; and the next one, the liner to the shell itself and the shell to the bone.

And some very simple but informative tests regarding pull-out -- as Mr. Noiles said, pull-out is not the basic way in which these fail but this is a relatively simple test that gives us at least a relative ranking of the ability of such a design to actually capture the head, and this gives us a very good idea. Because of the long clinical

history, it allows us to at least catalogue and get a feel for whether the design has been functioning well.

The testing that was done was a straight pull-out test of the head from the constrained liner and, essentially, after doing a few of these tests it was approximately 1300 Newton mean actual distraction load and, as Mr. Noiles said, compared to the Sivash, we pulled with a couple of tons worth of load to try and get a Sivash metal on metal pulled apart, and we brought the fixtures; we couldn't break the prosthesis and at that point we said, well, it is at least ten times stronger, and, you know, that was good enough for us at that point. It is orders of magnitude, like he said talking about the Eskimo numbers.

An independent laboratory also did an evaluation on the other interface, which is the cup-liner interface. And this is just a schematic. The results and reports are provided to you in the PMA submission. This is just to point out that the design that has been used since 1984 in the S-ROM -- it has been around for a few years. The interface between the liner and the shell is well proven. The way the liner interacts with the shell is that there are six types of polyethylene that mate with the shell and are rotated in places and give the liner itself its mechanical ability to withstand any kind of distractive loads.

Also, these devices are machined to very high precision and we do our very best, as demonstrated here whether there is only an apical dome hole or holes for screws in the dome at periphery, to demonstrate and to really provide as much conformity and support for the polyethylene because of the biomechanics of the hip joint, and as the independent laboratory concluded, the degree of conformity and support that is achieved in the J&J products may possibly reduce the generation of stress associated with wear debris because that liner is very well fixed within the cup and is very conforming and would tend to reduce the stresses, the contact stresses.

Now I am going to give a very light but, hopefully, complete introduction to the clinical information packet that we sent in. It is very important, as biomechanical engineers and clinicians, to keep track of this information.

The first thing we did, we went out and looked to what kind of patients, from the indications, would be using this device and it is people at high risk of dislocation and chronic dislocations. The literature gives us an average between 1 and 8 percent of dislocations after total hip arthroplasty and in some papers it could be as high as 25 percent even in the primaries, not just revisions. And

unstable joints can lead to many detrimental effects in the gait and the joint wear and possibly ultimately losing the prosthesis. So this is the framework under which we started to look where would this be used and why would it be used.

A paper by Vaughn et al. talked very eloquently about how to manage a chronically dislocated hip, not just with devices that are internal and surgical but also with external devices such as braces and other types of treatment, and they made some very astute comments here, very generic comments, that all methods of constraint have limitations, and we are aware of that, and there are different types of constraint, levels of constraint, but they all have limitations, but also by having all these methods available, these methods of constraint are successful in reducing the incidence of dislocation in a chronic dislocator.

Here is a summary of the patient series that we brought in. Essentially, we were able to find five papers in peer-refereed journals and conference proceedings, and the first author and the date is on the left-hand side; the number of cases. The next column is the follow up in months where applicable. Sometimes there were case studies but still you can learn from those. Then there was the number of

cases without dislocation. The column on the right gives us an idea of the percent of cases without dislocation.

The reason that I need to bring this up is because generically this device was used in these papers and was brought forth as a treatment for people that were at high risk for dislocation or specifically chronic dislocators already. So going into this paper, every single patient that had this implant put in them was a dislocator. So, in other words, the column on the right is very important. It is essentially 100 percent dislocators. And at worst case we have about 29 percent after the surgery and at best case, only 5 percent of dislocators. So dislocation rate went down drastically using the device.

Of the 194 cases reported, also after reading the papers and I'm obviously speaking to you after having read these and I am sure you would come up with the same common themes, the risk for dislocation of a chronic dislocator, and the fact that it was instability intraoperatively as well as preoperatively, surgeons looking for alternatives -- alternatives mentioned also being fusions, braces and other kinds of issues that could be used, not just a surgical device, and finding adjunct combinations that would give better stability, and ultimately in almost every paper

reports of patient selection and surgical technique was evident.

And a couple of general conclusions, for example from Cameron and his paper is saying that the indications for the device are limited, which I think the FDA and the manufacturers would agree with, but also that a device such as this is needed and has shown relatively good early results in the two to three-year time frame -- very generic conclusions.

And I am going to steal a little bit of the thunder from Dr. Wilson, who is sitting next to me and I will introduce him to you shortly, some very general but very astute observations that he deemed this as a very valuable tool for complex primary and revision hip surgery where there is a high risk for dislocation and, as you will see from his presentation, the potential benefits, definitely biomechanically and clinically, as he will point out, outweigh the potential risks.

In general, in the multiply operated patients and in the absence of some of the soft tissue mechanisms or patients that are at high risk for dislocation, sometimes a device such as this can be the only option to achieve initial stability and probably long-term stability.

Finally, the constrained liner offers the surgeon and the patient a viable alternative for repeated dislocation and instability and loss of mobility. So it is part of a continuum of constraint, modular. There is good clinical data out there showing its safety and effectiveness and the long clinical history is part of the support that we bring to you.

I would like to introduce now Dr. William Wilson, who will share some of his clinical experience with us today using this liner.

DR. BOYAN: I just would like to remind you, as you should begin Dr. Wilson, that we have 15 minutes left for the company's presentation.

Presentation by William J. Wilson, M.D.

DR. WILSON: Well, good morning, ladies and gentlemen. My name is William Wilson, and I am an orthopaedic surgeon in private practice at the Seattle Orthopaedic and Fracture Clinic, in Seattle, Washington. I am in no way affiliated with Johnson & Johnson Professional, Inc. other than that they have paid my expenses to come here, to Maryland to present this paper, which was initially put together to present at the North Pacific Orthopaedic Society meeting in Portland last year, and which has been submitted for publication.

Dislocation following total hip replacement can be a very complex and frustrating problem for patients and hip surgeons alike. This is especially true in cases involving multiple prior hip surgeries, soft tissue imbalance or muscle weakness, neuromuscular disorders, dementia, or revision surgery fro chronic instability. In situations such as these, the instance of dislocations has been reported to be as high as 27 percent.

In an attempt to reduce the risk of postoperative dislocation in complex cases such as these, we began in mid-1990s to utilize the constrained acetabular liner in patients who we thought were at excessive risk for this complication. This study then is a retrospective report of our experience with the use of such a prosthesis.

Seventy-four patients, 45 women and 29 men underwent primary or revision total hip replacement between October, 1990 and February, 1996 utilizing the S-ROM acetabular component with constrained polyethylene liner. This was a consecutive series of patients in which this liner was utilized by three separate surgeons. The patients ranged in age from 38 to 94, with an average age of 71.2 years. During this time 10 patients died and 3 others were lost to follow up, leaving 61 patients as the basis for this report. The average follow-up period was 25.9 months.

There were 4 primary total hip replacements and 57 revisions. Of the 4 patients undergoing primary hip replacement, 3 had a diagnosis of osteoarthritis and a concomitant neuromuscular disorder. One each was cerebral palsy, Parkinson's disease and Alzheimer's disease. The fourth patient had severe rheumatoid arthritis, was a marginal community ambulator and fell, sustaining a femoral neck fracture.

The indications for revision were recurrent dislocation or subluxation in 26; loosening or osteolysis in 3; status post-resection arthroplasty for sepsis in 6 and painful hemiarthroplasty in 3. You will notice this adds to more than 57, and in some cases there was more than one indication for the revision.

With regards to indications for use of the constrained liner, we had instability, recurrent dislocation or subluxation in 26; advanced AIDS 12; paralysis/spasticity 3; dementia 1; and muscular imbalance or weakness in 19. Within this last category there were 6 patients who were status post-resection arthroplasty; 7 who had weak or non-existent abductors to their multiple prior hip surgeries; 4 patients with long-standing trochanteric non-union could not be repaired; and 2 with severe debilitative rheumatoid arthritis.

Forty-two patients were able to come in for final follow-up exams, X-rays and computation of Harris Hip Scores. Nineteen patients either lived out of state or were too old or sick to return for follow up. These patients were contacted telephonically and answered complete questionnaires, as well as having local or home X-rays taken and sent in for evaluation.

The prostheses used in these patients were the S-ROM Arthropor cup initially until it was replaced by the S-ROM ZTT cup in about 1994. The specifics regarding the cup and the design have already been pretty well covered. So in the interest of saving time I will move along.

Of the 61 patients with a minimum of 6 months follow up, we had 3 that sustained dislocations. The average time from surgery to dislocation was 5 months, with a range of 2 months to 7 months. In each case of dislocation the acetabular insert remained seated in the shell while the femoral head dislocated. There were no instances of disengagement of the liner from the shell. In one case the metal locking ring had been be noted to have slipped off the insert labrum prior to the dislocation. In the other two cases the locking ring disengaged at the time of dislocation in one patient and remained seated despite dislocation in the other. All 3 of these patients underwent open reduction

with exchange of the acetabular insert and were very satisfied with their hips at the time of final follow up.

There were no cases where there was any evidence of prosthetic migration or loosening on final follow-up X-rays. We had 12 patients that showed evidence of non-progressive radiolucencies at the bone-cup interface, measuring no more than 2 mm. You can see the average cup abduction and anteversion there, which are well within recommended ranges.

Fifty-nine of 61 patients were satisfied with the results of their surgery at final follow up. One patient was unsatisfied because he could not walk. He had no pain and had not dislocated but he was extremely debilitated due to multiple chronic medical problems. The other patient was a chronic pain patient and X-rays on her revealed disengagement of her locking ring. She had been advised to have surgery to replace that locking ring but has refused to have that done. Thus far, she has not dislocated however.

Harris Hip Scores were calculated for 42 patients who could come in for final exam. The average Harris Hip Score was 82, with a range of 56-100. We had 26/42 patients that scored between 80-100. Only 1 patient scored below 60. This is a Worker's Compensation patient with chronic pain who has been off work for several years period.

Four patients scored between 60-69. One of these patients has no pain in his study hip but he has a girdle stone on the other side accounting for his low Harris Hip Score. Another patient had severe debilitating rheumatoid arthritis but no pain in her study hip. A third patient has chronic pain from trochanteric non-union, and the fourth is the unsatisfied patient mentioned previously with the disengaged lock ring.

There were no intraoperative complications. One patient grew coag. negative staph. on an intraoperative culture. This patient was 91 years old. We merely put him on long-term doxycycline and he has had no evidence of any ongoing further infection. We had 2 patients that developed deep infection postoperatively. One of these has since been revised for resection arthroplasty. The other is 96. He is on chronic suppression and he is infection free and pain free. We have one patient that required evacuation of a hematoma. We had two patients where a locking ring disengaged, one of which dislocated subsequently and we had one minor stitch abscess.

Of the 10 patients who died, 6 were followed for at least 8 months postoperatively. None of these patients dislocated and all were functioning satisfactorily at the time of their death.

I will show a couple of quick cases. This is the first case that I used this prosthesis on. This is a 93-year old resident of a nursing home, demented, who was a patient of one of my partners who went on vacation, and she came into the emergency room with a dislocated bipolar, as you can see on the left. Getting the history, this was the fourth dislocation in three months. Clearly, this was not working for her. I said, what am I going to do about this? And my partner was out of town and I said, what the heck, I am going to bite the bullet and try and fix this problem. I put a constrained acetabular component in her. She went back into the nursing home. She died six months later with no further dislocations.

This is one of the patients that had noted on the 6-week postop check a disengaged locking ring. This acetabulum had been revised for recurrent dislocations. So initially this was put in because of recurring dislocations. Six weeks postop we noted this. I said, that worries me. We had better fix it, and while he was waiting to have his surgery done to put that ring back on, he dislocated, as you can see there. We then did an open reduction and exchanged the liner and he has done fine since then. His Harris Hip Score at final follow up, now two and a half years later, is 100. He has no pain.

This is the other case of dislocation, a lady with severe rheumatoid arthritis who had this constrained acetabular component done because she was primarily a sitter and a very marginal ambulator, and she had her husband checking her cubitus on her peritoneum one day, hyper-flexing her hip about 140 degrees and dislocated, and she required open reduction and exchange of the liner.

Dislocat ion rates as high as 27 percent have been reported following revision total hip arthroplasty. Numerous factors can increase the risk of dislocation, including both patient and technique-specific factors. Despite closed, such as bracing or casting, or even open treatment, such as repositioning the components, lengthening the components, removing impinging structures, recurrent dislocation rates after revision surgery for instability can be as high as 28 percent.

We have had similar frustrations with this c omplex problem. Patients also can become extremely frustrated, at times becoming so frightened of another dislocation that they are almost paranoid and afraid to do much of anything. I have one patient that wore his brace continuously for six months, only taking it off to bathe. He wouldn't even take it off in bed because he was afraid he was going to dislocate. We ultimately revised him with a constrained

liner. He has had no further dislocations and he is very happy.

So following the initial use of the S-ROM constrained acetabular component in the first patient that I described above, we began to use it in other patients with a history of recurrent dislocations. After several cases and no problems we began to use it a little bit more indiscriminately. Then we had three dislocations and we decided that we needed to look at this a little bit more careful in terms of what the indications for use of this liner are.

We have come up with these indications: Recurrent dislocations, neuromuscular disorders, dementia, multiple prior surgeries, trochanteric non-union and advanced age or chronic illness. And it is in these last three categories that we need to be a little bit more careful in our indications. I am still -- we still are proponents of this prosthesis, and I believe strongly that without it we would have had many more dislocations in this group of patients. However, the need for open reduction following dislocation of this prosthesis is certainly a drawback and this should keep surgeons from utilizing it indiscriminately.

I now recommend that in those cases where there is a serious concern regarding potential for dislocation, but

no absolute indication for the use of the constrained liner, that the revision of the acetabular component be done utilizing the S-ROM ZTT shell and then a standard, semi-constrained liner. That way, if problems with dislocation do occur postoperatively it is a very simple procedure to exchange the standard liner for a constrained insert.

There is one other theoretical drawback t o the use of the constrained acetabular liner, and that is the potential for increased forces transmitted to the interfaces between the liner and the shell, and also the interface between the shell and the bone. There have been a couple of isolated reports of disengagement of the liner from the shell. The exact incidence of this complication is not known. We did not encounter any instances where the liner disengaged from the shell.

Whether wear or fatigue may lead to problems with disengagement later on and further follow up remains to be determined. Loosening at the prosthesis-bone interface was not seen in our group of patients, nor has it been reported elsewhere in the literature when the S-ROM porous coated acetabular shell is used. None of our patients showed any evidence of prosthetic migration or significant radiolucencies, or any significant osteolysis.

I will just conclude by saying that after experience with the S-ROM constrained acetabular insert in now over 80 patients over 7 years, and minimum 6-month follow up on 61 of these patients, we believe that this prosthesis is a very valuable instrument in the armamentarium of the surgeon performing complex primary and revision hip surgery.

We also believe that when proper indications for the use of this prosthesis are followed as outlined above, the potential benefits of this prosthesis far outweigh the potential risks involved with its use. Indeed, use of a constrained acetabular component provides the only really viable alternative in many of these complex cases.

Thank you. I will turn things back over to Sally Maher.

Closing Comments, Sally Maher, Esq.

MS. MAHER: Thank you very much. The one thing I wanted to leave you with, and we really appreciate your patience in hearing us through and I know we were longer than normal, was that this is a well-established product with a strong clinical history, and there is absolutely no evidence that t here are any safety or efficacy issues or concerns. We think that the data we presented in the PMA

strongly supports an approvable recommendation from you all, and would just thank you all very much for your attention.

DR. BOYAN: Thank you very much. There has been a suggestion from the Panel that we have the FDA presentations immediately following you all and then have a general discussion after that. If that is acceptable, why don't we move over to the FDA presentation? The lead reviewer is Hany Demian.

FDA Review, Hany Demian

MR. DEMIAN: Good morning, ladies and gentlemen. Madam Chair, distinguished Panel, members of the audience, I am Hany Demian, a reviewer in the Orthopaedic Devices Branch.

The PMA product under consideration is the Johnson & Johnson Professional S-ROM Poly-Dial Constrained Liner. I would like to thank Johnson & Johnson for their presentation and tell Dr. Noiles, being from the younger generation, that history does repeat itself. So we have a lot to learn from him.

The review team for this submission consisted of myself as lead reviewer, Dr. Stephen Nightingale, to the right of me, as the clinician, and T.C. Lu as the statistician.

Today our presentation will be brief. I will describe to you the proposed indication for use, the device description, and the preclinical studies. Dr. Nightingale will present the clinical studies. Then I will come back and present the Panel questions.

This is the same indication for use that Johnson & Johnson has presented so I won't read this but just show it to you.

The device consists of ultra-high molecular weight polyethylene constrained liner that fits into various metal shells manufactured by Johnson & Johnson. The constrained liner is assembled in surgery. The polyethylene liner is held in the metal shell with bone screws. The liner has a slight equatorial overlap which allows the femoral head to be snap-fit and mechanically captured. This polyethylene liner overlap is reinforced with a titanium alloy ring.

The S-ROM Poly-Dial Constrained Liner is available in 0 and 10 degree offset designs. This liner is available for use with a standard Johnson & Johnson metal shell. Note that the Arthopor series must only be used with bone cement.

The constrained liner has a minimum thickness of 4.3 mm. It has an outer diameter ranging from 36-57 mm, and a standard inner diameter of 28 and 32 mm corresponding to

metallic femoral balls. Note that 26 and 29 inner diameters are available upon request.

The applicant provided the following preclinical studies. I will just give the highlights here. There was information about validated gamma radiation process that has been used. For shelf life, Johnson & Johnson has provided sealed strength testing and dye penetration testing which support a shelf life of five years. Both materials used in this design, that is, ultra-high molecular weight polyethylene and titanium, have a long successful use in semi-contained total hip arthroplasties.

I will discuss mechanical testing next. The applicant determined the force necessary to distract the femoral ball from the polyethylene liner. The average distraction force was 274 lbs., or 1219 Newtons.

In addition, the applicant supplied incongruity analysis in which the amount of metal-supported polyethylene was measured in an unloaded condition. The results showed that the metal shells with more holes provided less support to the polyethylene liner.

I will now turn this presentation over to Dr. Stephen Nightingale for the clinical studies.

FDA Review, Dr. Stephen Nightingale

DR. NIGHTINGALE: Thank you very much. The clinical data submitted by the applicant consisted of the five publications that are on this slide. The first two publications were substantive. The third, you have already heard a bit from Dr. Wilson. I would apologize here to Dr. Wilson for reversing the order of his initials. But, unfortunately, it was not I who did this. If you will look at page 59 of the PMA submitted by the sponsor, reference 8, it was, in fact, the sponsor who reversed Dr. Wilson's initials --

(Laughter)

-- so I do not take full blame for that. We both apologize to you, Dr. Wilson. Dr. Wilson's presentation was available to me only in very brief detail at the time I prepared this review. Dr. Fisher et al., and Cameron et al., comment on the use of the device but the major focus of my review was on the first two articles.

The patients in these two articles are summarized on this slide. You need to note that there are 57 procedures in 55 patients in the Lombardi et al., article, 21 for 21 in the Anderson article. There was one case in Anderson et al. that was analyzed further because it was not a relevant patient, the patient died from unrelated reasons.

But the reason for pointing out the distinction between procedures in patients is to extract the data from this study. Sometimes the data is in terms of procedures and sometimes in terms of patients. What we do have in the remaining rows of this slide is a comparison of the patients. You can see that they are roughly comparable, with a mean age of 69 in the Lombardi series, 66 in the Anderson series. The sex ratio is identical. Almost all of the Lombardi series had previous procedures and the majority in the Anderson series. And you can see for those who had a previous procedure, there was an average of 2.3 procedures for those patients, with a range of 1.6. In the Anderson series there was an average of 2 procedures, with a range of 1-4. We consider these patients roughly comparable.

The underlying diseases in the patients were not identical but I think comparable. Osteoarthritis in the majority of the cases, not patients, in the Lombardi series; almost a majority in the Anderson series. One of the patients, as you see in Anderson, was post-sepsis but, again, I describe these for your interest. We found them, again, to be roughly comparable.

The indications for the constrained device, again, differed but differed in degree rather than qualitatively. Prior dislocation was the indication in the majority of the

patients in the Lombardi series and in almost all of the patients in the Anderson series. Again, there were a small number, 6 in the combined series of patients, who had intraoperative instability as the indication for the device. The other indications given are joint laxity, either neurologic or muscular, femoral fracture, aseptic necrosis and conversion of arthrodesis were the indications for this constrained liner.

The meat of the analysis of these two studies is on this slide, which describes the patient outcome. You can see the mean follow up in months was comparable for the two series, and subsequent dislocation -- I give the exact numbers there, and this is in terms of patients for the Lombardi series, 5/55, and for Anderson there were 6/21.

You can see the final Harris Hip Scores are given, 67 and 76 for the two series, with the ranges that you see up there. And for patients in whom there was radiographic evidence available, which was almost all of the patients, 48/50, had a stable acetabulum in the Lombardi series and all of the 21 patients in the Anderson series.

The details for the dislocations for the Anderson series are given in the fine print down below. Three of the patients had two subsequent dislocations and two of the patients had one subsequent dislocation. At the bottom of

that bottom line is that four of the five patients who had dislocations were ambulatory at their last follow up.

These are the studies in which I had limited clinical information to work with. You have heard a more extensive description in Dr. Wilson's series. The information that I had to evaluate is on this slide, 61 cases, with a mean follow up of 26 months and 3 dislocations.

The remaining two papers, Fisher and Kiley, and the Cameron paper, Fisher and Kiley described a dislocation but stated in their experience they had only five dislocations in 51 cases, and Dr. Cameron, again, did not state his follow up but he stated that there were no dislocations in his six patients. We don't have further information from Dr. Cameron.

Regarding adverse events, as the sponsor has noted, this has substantial volume -- approximately 1000 units were sold in 1996. Both the sponsor and we collectively and independently identified 25 Medical Device Reports. As I said yesterday, identification of Medical Device Reports is not a simple procedure. I can say that what we did in this particular case was we searched our own database in three different ways: We searched it by manufacturer; we searched it by a description of the device;

and se searched it by a variety of product codes which have three-letter acronyms which are familiar to us but probably not to the public at large, and I can describe that search in more detail, but the bottom line of it was that we came up with the same data that the sponsor came up with in. In particular, other than dislocations, the only two descriptions of clinical events that we identified in this search were the two that are on the slide, which is that in one patient the liner wore through and the Medical Device Report states that the patient was very active, a professional ballet dancer who also hikes and bikes. Again, according to the second description, lock pins were alleged to have released allowing the ultra-high molecular weight polyethylene insert to rotate and dislocate. We have no other information on adverse events.

MR. DEMIAN: Thank you, Dr. Nightingale. I will now present nine Panel questions which the Agency is seeking recommendation for this PMA.

Is the following proposed indication for use supported by the PMA information for the subject device? Again, this is the same indication that we have shown earlier.

If this indication statement is not supported, what would you recommend?

What are the appropriate contraindications, warnings and precautions for this device?

Should the indications be limited in any way?

Should there be limitations on the usage of the device for certain patient populations?

Based on the data derived from the clinical studies or other sources of adequate scientific evidence for the S-ROM Poly-Dial Constrained Liner, are specific clinical evaluations or tests needed for the selection of patients for this device?

Because of the constrained design of this device, should there be any special instructions for the short- and long-term patient management, including activity restrictions?

Should any additional or special instructions be added to the surgical technique for total hip arthroplasty when using the S-ROM Poly-Dial Constrained Liner?

Lastly, is a separate patient information sheet necessary for the S-ROM Poly-Dial Constrained Liner? If so, what types of information should be contained in a package information sheet?

Thank you. I will now turn this back over to Miss Barbara Boyan.

DR. BOYAN: Thank you very much. At this point I would like to give everybody a chance to take a ten-minute break, and when we return we will have general discussion. Thank you.

(Brief recess)

DR. BOYAN: The FDA have had a chance to ask what it is that they would like to ask specifically. Some of those questions may have generated sine more discussion and we will open it for general discussion, and after that process, then we will go to see if the Panel is ready to make a motion. So for the Panel discussion -- this is now just asking questions, not the motion, I would like to start with the lead reviewer, who is Dr. Greenwald -- make your review. Pardon me.

Panel Review, Dr. A. Seth Greenwald

DR. GREENWALD: Thank you, Dr. Boyan. My name is Seth Greenwald. I have been asked to be a biomechanical lead reviewer for the Panel, and my clinical colleague, Dr. Rudicel, will then follow with the clinical review.

Much of what I will read to you has essentially been said or alluded to but for the benefit of the Panel and for the sense of completeness, I have written out my remarks and I will enter these into the record.

Biomechanical Review, Poly-Dial Constrained Liner (S-ROM): Numerous conditions affect the functional integrity of the soft tissue envelope in complex revision hip arthroplasty that can predispose the patient to inherent dislocation.

Clinically the problem of recurrent dislocation has been addressed by trochanteric advancement, larger femoral head size or bipolar insertion, elevated rim liners, component repositioning, spica cast or orthotic bracing, fusion and girdle, as well as the use of constrained liners.

Particular to the latter, the S-ROM Poly-Dial Constrained Liner consists of an ultra-high molecular weight polyethylene acetabular liner and a titanium alloy locking ring. During assembly, the former snaps into a metal shell and is held in place by a circumferential bayonet locking mechanism which allows complete retention of the liner beyond its equatorial plane and extended polyethylene labrum. Peripheral locking screws and/or pins secure the liner in a required position. The constrained liner is supplied with 0 and 10 degree offsets and also demonstrates a peripheral chamfered lip which serves to accommodate the locking ring during femoral head assembly. Prior to assembly the liners are stored in a freezer to allow a shrink fit.

The resistance of the assembly to dislocation was measured by direct pull-out testing for various socket and head tolerances, with the worst case separating at approximately 270 lbs.

A further evaluation describes shell-liner conformity for both the one- and four-hole assemblies which ranged between 66 to 68 percent and 55 to 58 percent, respectively. This demonstrates a moderate degree of conformity in relation to other contemporary modular acetabular components and should assist the reduction of stress-associated wear debris over time.

These tests are supportive o f the clinical experience with the device, although by no means replete, and these questions I now address to the sponsors: Have the sponsors carried out more than three dislocation tests? Have dynamic, but particularly impingement evaluations, as inferred in the Cameron article -- these valuative deficiencies not withstanding, these tests are supportive of clinical experiences with the device.

Clinical experience indicates that the majority mode of failure was femoral head predominantly or in a couple of instances liner separation, an occurrence which predominates in 17/25 filed MDR reports.

Given the limited indication for the use of constrained sockets, but significant need when indicated, the number of complaints received between 1992 and 1995, 41 by count, in relation to approximately 6747 units sold, appears minimal. Although not an absolute -- that is, MDR being not an absolute, it does suggest an acceptable risk when this device is used.

Thank you.

DR. BOYAN: Thank you, Dr. Greenwald. Dr. Rudi cel, would you like to give us your review?

Panel Review, Dr. Sally Rudicel

DR. RUDICEL: I am Sally Rudicel. I don't have a lot to add to the clinical review that was presented. We are dealing with a small number of patients here but this is a small population that has this problem. The results in other studies on revisions have shown anywhere up to 19-20 percent of dislocations, and in the studies that were presented here we have a 4.9 and a 4.5 redislocation rate, and in one study 29 percent redislocation rate. But I think you have to consider the patient population.

I think that the studies that are presented do show that there is an indication for this procedure, and that it is an effective procedure, and that the

complications are not beyond those that would be expected in this patient population.

There was also in the papers presented a trend of increasing failure with the device in patients who had had increasing numbers of operations, and so that also is as one might expect in this difficult patient population.

So I think that the articles do show us -- and also the fact that this device has been in use for such a number of years -- that there are clear-cut indications and that the failure rate is within what might be expected for this particular population.

Also of note, there have not been reported instances of acetabular loosening, which one might expect with this device. We clearly know that patients will loose range of motion but the Harris Hip Scores have been acceptable.

I think the othe r important point to glean from the literature is that this is a technically demanding situation, that the surgeon needs to be quite careful in the patients that they select, and that surgical technique is important, and the device labeling has gone along with this to indicate what surgeons need to do for this.

DR. BOYAN: Thank you. Now let's start back over with Dr. Skinner and just go around the room and address

questions. Questions may be addressed to the presenters from Johnson & Johnson Professional, Inc., the FDA reviewers or however you want to handle it.

DR. SKINNER: Harry Skinner. Dr. Boyan, can I ask more than one question?

DR. BOYAN: Yes, you can.

DR. SKINNER: Thank you. Could I ask someone from J&J a couple of questions? First of all, the slide showed a 29 mm head. I assume that is a typo.

DR. BOYAN: Before you speak, could you state your name and your affiliation?

MR. OCHOA: My name is Jorge Ochoa, R&D manager for hips at Johnson & Johnson Professional. That is not a typo. Actually, one of those was produced on a special for revision of a patient that was a candidate for this type of procedure but presented a femoral head on a stem that was 29 mm diameter. So actually it was special, that one case.

DR. SKINNER: Okay. As long as you are there, regarding head size, I didn't understand why ceramic heads were contraindicated.

MR. OCHOA: At that time they weren't in the original 510(k) submission so we couldn't pair them, one with the other, because ceramic heads came later. So that has not been upgraded yet so it is an issue of chronology.

DR. SKINNER: It is not an intrinsic factor of the ceramic head then --

MR. OCHOA: No, sir.

DR. SKINNER: -- it is a regulatory --

DR. OCHOA: Exactly, timing; having one catch up with the other.

DR. SKINNER: You mentioned tolerances regarding total hip heads from other manufacturers as a relative contraindication. Is that what you implied? That the tolerances for a femoral head from another manufacturer might not be -- it, for instance, might be smaller so the pull-out strength might be less. I think that is what you were implying.

MR. OCHOA: Well, actually, the contraindications are that when necessary -- well, the specific contraindications state that the devices should be matched by manufacturer but there are multiple issues that could transpire if they are not, and without having that data at hand at every single point there could be some complications.

DR. SKINNER: Do you feel that this is something that should be specified in the package insert for the benefit of the orthopedic surgeon?

DR. OCHOA: It is currently specified in the package insert.

DR. SKINNER: It is implied only for an S-ROM Joint Medical Product/J&J head.

MS. MAHER: I would like to answer that. My name is Sally Maher. We believe, as a manufacturing company, that our products are only -- they are contraindicated to be used with other manufacturers' components because we have no control over the tolerances or anything else. We do specify and provide the information as to the size of our products. However, we do state in our labeling very clearly that these products are only to be used with other J&J products.

DR. SKINNER: Despite the fact that it is indicated for revision procedures where the femoral head might be from another manufacturer?

MS. MAHER: That is correct.

DR. SKINNER: Regarding the locking ring on the plastic insert, is it stated in the package insert that the locking ring should be used only one time, and does it imply or state that you should replace the plastic if you take the metal ring off and try to put it back on, or is that a factor?

MR. OCHOA: The package insert in general states that the device, once used, should not be reused or

resterilized. So generically it is there because we have that position, and Sally can elaborate on that for all the implants. It is not specifically stated, I believe, for the specific ring on that specific device. So it is not specific to that device but in general it is stated across the board for all devices.

MS. MAHER: That is correct. Our insert generically states that -- our package insert, excuse me, that once an inserted liner is put in and then taken out you need to open a new one and put a new one in, and that goes with all the other components of an implantable device, and that would include then the locking ring.

DR. SKINNER: So that if it was placed and the patient was put through a range of motion and you decided that it needed to be changed, you should take the plastic out, put a new plastic in, and put a new retaining ring in.

MR. OCHOA: If it needs to be changed, yes, sir, because that would be the reason. The new plastic would come with a new ring. They come packaged together. So if the surgeon determines that they are going to change the liner, when they open a new liner a new ring will come with it.

DR. SKINNER: It is, of course, very important to make sure that the locking ring goes in the appropriate direction. I notice the package insert specifies that.

Perhaps a label, some sort of little paper ring around it pointing in the direction of the patient, or something, would be helpful because that is a crucial point in the placement of the ring.

MR. OCHOA: Yes, sir.

DR. SKINNER: Regarding range of motion, for instance, with the 28 mm head without a skirt, what would be the maximum range of motion that could be obtained? Arc of motion is what I am talking about.

MR. OCHOA: Yes, the arc of motion, about 100-degrees.

DR. SKINNER: A hundred degrees?

MR. OCHOA: Which is a littl e bit -- comparatively speaking with a semi-constrained -- upwards of 115, 120 degrees.

DR. SKINNER: I have a couple of other questions but I know Dr. Markolf is going to ask them so I will give him the chance and if he doesn't ask them I will come back.

DR. BOYAN: Okay. Dr. Greenwald?

DR. GREENWALD: I would like to pick up on a commentary that Dr. Skinner made. I think the labeling perhaps ought to be re-reviewed to make absolutely certain that if a liner is snapped into place, the femoral head is locked through the use of the retaining ring, taken through

a range of motion and then, for whatever reason, the surgeon decides to remove it, that it should be in plain and simple English that that liner and that ring should be replaced because once on, it is never the same. The polyethylene has been compromised. And I think there are a number of studies in the literature that support that contention. I think if it is not clear in the labeling, as I think Dr. Skinner was perhaps alluding to, clear to his mind as a surgeon, it certainly should be made clear because I think that is a very important factor regarding longevity of the device.

Now, I wanted to pick up on a couple of other questions that I brought out in my review. I was a little struck by the reporting of but three pull-out tests. Now, certainly that is a pretty minimum number. Different tolerances were used between the liner and the head itself to come up with an optimal interference fit. And I just wondered whether or not further tests had been run. And I recognize this is after the fact because who is going to argue with almost ten years of very satisfactory clinical results but, nevertheless -- and maybe Mr. Noiles can answer these questions because I realize it was back then -- number one, was an impingement test run? They were alluded to by Dr. Cameron in terms of inch-pounds or pound-inches. And I

just wonder whether or not any other tests had been run to establish impingement resistance levering out.

MR. OCHOA: I can answer some of the mo re recent history, and I think Mr. Noiles can answer some of the prior history before Johnson & Johnson acquired Joint Medical.

The first thing I want to clarify is that even though three tests were done in that report that was submitted, we didn't specifically pick different dimensions on the diameter on the actual dimensions to prove anything. We took three off-the-shelf devices and tested those.

We have done some tests recently and we uncovered these because they were done for different reasons. We were actually testing femoral head components and ended up using an acetabular component that happened to be the constrained component. So in our first search when we were looking for constrained liner we missed it because it was femoral head testing.

But we did do testing. We did a few more pull-out tests and the numbers -- I don't have the details -- were right around the same and the standard deviation was approximately the same. And we did do some impingement testing and Mr. Noiles can address some of the historical numbers. He quotes numbers in the vicinity of 150 inch-pounds and, without having the exact comparison and exact

lengths, we came with numbers that were closer to the 180 inch-pound range -- similar enough, in my mind, without having the benefit of the historical details, to be not too worrisome, and similar enough that we were comfortable with that number, the issue here being, you know, how much is enough? And to your point, Dr. Greenwald, the ten years that we have up till now tells us that more or less 150-180 inch pounds seems to be about enough.

DR. GREENWALD: Okay. Well, I think going right along those lines, I want to suggest to you that you do not want to become the victims of your own success. And as time goes by with an increasingly successful patient population whose activity levels are going to vary from predominantly probably very, very seldom used or articulated to any great degree to perhaps more frequent articulation in a more active patient, and I just wonder whether or not there might be -- in fact, I don't wonder, I think there probably would be some direct advantage to dynamically, in a test rig, cycling the device to a range of motion and then ultimately at a million, two million, three million cycles perform impingement experiments so you have some threshold of anticipated failure because take the worst case situation when you are dealing with an active patient, it would seem not illogical to try to establish some minimal threshold and

a doctor, physician or surgeon may, in fact, in a routine re-exam of a patient be wondering just how active that patient is, and are they approaching that potential threshold of articulation. Just a comment. I wondered -- I don't know if Dr. Noiles is going to comment on that but it certainly struck me -- again, I am saying these are after the fact but, as I say, you don't want to become a victim of a successful device over a long period of time.

I would like to get a little philosophical explanation from Mr. Noiles, if we could. I was really intrigued, and it is a logical design evolution, that the fail-safe mechanism should be dislocation of the head from the liner; secondly, the liner from the cup; and lastly, the shell from the bone. The latter -- I think I came across one incident of where that had happened in a cemented cup, and I just wondered what your logic was. Did you do any calculations, Mr. Noiles, on what it took to dislodge the shell from the cup and the cup from the bone? How do you arrive at that worst-case scenario for us?

MR. NOILES: There are two guiding principles. One, the cup shouldn't come out of the bone. That is the starting point. Now, the value of that retention is an unknown. Secondly, the ball shouldn't come out of the insert. That is desirable but perhaps not attainable.

We didn't design it specifically in a one, two, three sequence. It came out that way. It really doesn't matter to the patient or the surgeon whether the ball comes out of the insert, or the insert comes out of the cup. You have to replace it in either case. But it was fortuitous that it came out that way.

DR. GREENWALD: Well, it might mean something to the patient if the cup came loose against the bony bed and it wasn't a frequently encountered situation until you accelerated either a lytic situation or strain pain. It is probably going to hurt in all instances but it just might hurt more. It is likely it would be a worst case scenario, as you pointed out, if the cup is dislodged from the bone.

MR. NOILES: Oh, yes, yes. I guess what you are leading up to is that I can say that we don't know how high we could go with the constraint of the ball within the plastic. Could we increase that? Now, the first thing you do is reduce the range of motion a little bit, and that is kind of negative. The second thing is we want the surgeon to be able to put it together in the operating room, and as you make more constraint it becomes more difficult for the surgeon. So it is just a balance of things there.

DR. GREENWALD: I guess I would have to call it SWAG, scientific wild anticipated guess. Nevertheless, you can't argue with success.

MR. NOILES: You know, if you are guessing at it for 25 years you have a number of shots at this thing --

(Laughter)

Then part of your other question, you were talking about tolerances. In the early history we tested a whole range of tolerances of the ball and the socket. As a matter of fact, it happened to be a manufacturing engineer who ran the test and he came back and said, gee, we can loosen up the tolerances a little bit because this thing looks adequate and the change is not too much. But we didn't do that. We elected to stay with the best we could make.

And I do want to comment on other manufacturers' heads. You saw a ballet dancer who wore through the plastic. It was the head of another manufacturer. It was cast cobalt chrome. We got the head back with the insert and there was porosity in the head. So what the company says is we like this thing to be used with our products; we know what they are. Our heads are good; our tolerances are good; our finishes are good. But to use somebody else's, that is your responsibility. Of course, they do get used that way.

DR. GREENWALD: Thank you.

DR. BOYAN: Thank you. Dr. Rudicel?

DR. RUDICEL: I don't have any further questions.

DR. BOYAN: Dr. Rangaswamy?

DR. RANGASWAMY: I just have a comment, actually, to commend Dr. Wilson, that when he gets his paper somewhere that it does put in the fact about the learning curve, and when he had those patients with a problem with the dislocation that occurred that you went back and decided maybe you should look at the data, and maybe that is a word of caution to advise others to look at because people tend not to do it.

DR. BOYAN: Dr. Besser?

DR. BESSER: I have no comments.

DR. BOYAN: And Dr. David Nelson?

DR. DAVID NELSON: Just one minor series of questions and possibly Jorge Ochoa can answer me. Why do you think the ring dislocated in the one that you had? How did you handle that internally, and have you changed anything?

MR. OCHOA: We haven't changed anything. And out in the field we are, obviously, looking at product improvements but that is all an internal thing. As Dr. Skinner pointed out, figuring out why this ring dislocated -- it is only speculation. As he said, if you put it in upside down it will have less strength than if you put it in

right side up. And another thing is to obtain the balance that Mr. Noiles was talking about. Unless you have a fully metallic joint, which is, you know, really constrained, polyethylene has two inherent things in it: It is much softer than the metal, number one; and number two, the dimensional stability, no matter how high a quality polyethylene you have, the range is much different. So it is very difficult -- you know, we can machine with very high precision but the motion of polyethylene is inherent so it could be something that is environmental, to something that is technique related, to something that is just failing to function. So it would be speculation. And we are aware of these instances.

The good thing, once again retrospectively to what Dr. Greenwald said, these cases of the ring not functioning are few and far between, but it is something that we are looking at.

DR. DAVID NELSON: Well, certainly failure analysis is almost always speculation but that doesn't mean that is bad. For instance, it is funny when surgeons use the term single insertion only, it means you can't put it in one patient and then decide it didn't work and then put it in somebody else.

MR. OCHOA: Tha t is right.

DR. DAVID NELSON: It doesn't mean put it in once, pop it out and then not put it back in again. So the phraseology needs to be different than single-use only because that is not what single-use only means.

MR. OCHOA: Yes, sir.

DR. DAVID NELSON: Okay, thank you.

DR. BOYAN: Dr. Markolf?

DR. MARKOLF: I would like to go back to the philosophical issue here in your design goal. You said that really the bend-out strength of a cemented acetabular cup is unknown. I would submit that wouldn't be too tough to measure in a cadaver, twist it out to get an upper limit to see because your device is really a safety fuse. You want to protect that interface. So you want something to fail before that one does, but you don't really know what that goal is, and I just wondered had you considered, you know, doing any cadaveric tests. Granted, you know, it wouldn't give you an absolute number but it would put you in the ball park because, right now, for your device I am not sure what the bend-out is. You mentioned that would be the mode of failure and I think Cameron quoted something like 150 inch-pounds. Again, that data was not presented in the material provided to us. So, again, what is your philosophy on that? And where did those numbers come from?

MR. NOILES: Well, you are absolutely right that you can establish upsetting torques in the cemented cup in the acetabulum. Now, is that applicable to a living person? Well, it is better than anything else we have. I admit that.

The upsetting torque to come out of the plastic, 150 inch-pounds -- these are physical tests and they are lost in antiquity.

DR. MARKOLF: They are history?

MR. NOILES: They are history, yes. They were tested in United States Surgical. They were tested in Joint Medical Products which is now owned by Johnson & Johnson. Some of the papers went to a big warehouse in New Jersey, called Iron Mountain or something. Remember, there was a tremendous fire?

(Laughter)

Some of our records were lost there. Yes, there was a tremendous fire somewhere in New Jersey within the last two months I think, three months.

DR. MARKOLF: But it might be relatively simple to, you know, repeat that test --

MR. NOILES: Oh, sure, and it has been repeated --

DR. MARKOLF: Well, I haven't seen it presented.

MR. NOILES: Right, you are right.

MR. OCHOA: In some of the ongoing product development projects we have and product improvements -- I think all you ladies and gentlemen must have been sneaking into our product development project list, but that is important because one of the things that is stated with this type of device is the use of the peripheral screws, and the peripheral screws would add, regardless of the site, whether it is cemented or not cemented, those peripheral screws wouldn't interfere because they are outside; they are on the very periphery. And that is one advantage and one necessity for this constrained liner because of the biomechanics -- you are absolutely right -- to put those screws in there because the screws are not holding the polyethylene in place. What is holding the polyethylene in place is the bayonet equatorial ring. The polyethylene slips into a ring inside the substrate cup. Those screws are locking tabs. They just keep rotational stability. But by using screws instead of peripheral locking tabs, you dig into the bone and then, to your point, I think there is a test that they were doing and recording in a sense to get a feel for how strong is that interface. Going back to what Dr. Greenwald was saying, you know, let's push the limit; let's force rank them, and once they are force ranked let's see how high we

can take that force ranking to increase mechanical performance, and that is something that is in our minds.

DR. MARKOLF: Yes, I think it should be more than in your minds. I think it should be executed.

MR. OCHOA: Yes.

DR. MARKOLF: While we are talking about the insert of the plastic component into the shell, I noticed in your product information here that it recommends that you can either use the screws or locking pins. Can you describe the situations in which you would use screws and locking pins? It seems like the locking pins would come out easier. I am sure you can appreciate that, you know, what you can put together the body can spit right out at you, and I am just wondering what are the indications for the screw device and the locking pins.

MR. NOILES: Well, I think the indications are that some surgeons don't like screws.

DR. MARKOLF: Do you think they have the same degree of mechanical retention?

MR. NOILES: Well, Jorge said that the function of the pin or the screw is simply to keep the insert from turning. The insert goes in; it is rotated a twelfth of a turn. That is the mechanical strength. There is a little nick in each of the lugs and we recommend at least two

screws or locking pins to prevent them from rotating out from under the retention.

DR. MARKOLF: I understand that. What I am concerned about is those becoming dislodged --

MS. MAHER: Excuse me --

DR. MARKOLF: Yes.

MS. MAHER: Actual ly, our caution statement in the insert, and this is a generic insert that we use for different pieces with different parts -- excuse me, I am Sally Maher; I forgot to introduce myself. But we specifically state as a caution use only S-ROM peripheral screws to lock the position of the constrained liner. Locking pins should not be used because they may prevent correct assembly of the reinforcing ring. So we specifically call out in our insert to use the screws, not the locking pins. It is a little confusing I think and we might need to clean it up some because of the fact that this liner is used with other cups, and everything else, and the other cups with the semi-constrained can use the locking pins.

DR. MARKOLF: Well, why offer locking pins at all, you know, if you are recommending screws?

MS. MAHER: We offer the locking pins for use with the semi-constrained liner.

DR. MARKOLF: And right now they share the documentation.

MR. OCHOA: Absolutely.

DR. MARKOLF: You just might simplify things because there is a chance the surgeon is going to pick the wrong thing for the device and not read the instructions --

MR. OCHOA: To segregate them out.

DR. MARKOLF: Also that locking ring, when you mechanically slip it on is there a snap fit on that? What keeps that from dislodging? Because I notice clinically there have been a number of dissociations in the referenced articles here. When you slide on that ring does it snap on? Is there a little shoulder that holds it in place to keep it from coming back off again?

MR. OCHOA: Yes, sir, and it is a slight press fit to hold that in place. Because of some of these rings falling out you may argue that there is not enough of a shelf or enough of a press fit, but there is an actual mechanical interlock between the rings. It is not just slipped on; there is a mechanical interlock.

DR. MARKOLF: Have you given some thought to looking at that in view of the ring dissociations that you have seen?

MR. OCHOA: Absolutely.

MR. NOILES: May I add to that and comment on some of Dr. Skinner's question? The ring goes over essentially a bar, and the ring is directional. It has an internal chamfer to help it over. And it is my own feeling that a surgeon ought to sit at his desk and put one together before he goes into surgery so he knows what the part looks like, and when it slips on there is a very tactile click so he knows it is fully on. It is entirely possible that at least one of those rings that came off was never fully on. Further, there must be no soft tissue under the ring. And trying to put it on backwards will not help the situation.

DR. MARKOLF: Is there some way you could provide, say, a sample or something for the surgeon? Because right now the only way he would have to practice would be on a sterilized component -- and big dollars!

(Laughter)

MR. NOILES: I can't speak to the present practice but that certainly has happened in the past, that we provided demonstration models --

DR. BOYAN: Are you going to make a comment directly to this because maybe, Keith, we should go around and then we can come back to that.

DR. MARKOLF: Yes.

DR. BOYAN: Is that acceptable?

DR. MARKOLF: Sure.

DR. BOYAN: Okay. Dr. Roger Nelson?

DR. ROGER NELSON: I know we are dealing with a lot of surgeons and once the surgery of a device is in we assume that the patient can sometimes get up off the table and move around without any intervention by physical therapy, and such, and often we tend to forget the patient. And what I would like to do is maybe bring a little discussion back to the patient.

Dr. Wilson, just a question, you said patients were satisfied with the device. I wonder how you obtained that information. Was it a question from you, or was there a standardized questionnaire type of question?

DR. WILSON: There was a standardized questionnaire that all 61 of the patients answered, and on that questionnaire there was a question that said, "are you satisfied with the outcome, or are you dissatisfied with the outcome?" And that is how the 59/61 came about.

DR. ROGER NELSON: Okay. So in other words, you didn't ask the person directly; it was asked on a questionnaire.

DR. WILSON: It was asked on a questionnaire.

DR. ROGER NELSON: The only other thing I would ask is did you look at any gait patterns and things like that?

DR. WILSON: I did not, no.

DR. ROGER NELSON: Okay. The only other thing I would probably ask for is, again, this issue of looking at the more health-related quality of life kinds of issues that are associated with the devices, and such, and implore the individuals doing the research to look at the issues of either gait patterns in a simple kind of fashion and/or the issue of standardized valid and reliable kinds of health-related quality of life kinds of issues. But that is all I have.

DR. BOYAN: Dr. Silkaitis?

DR. SILKAITIS: I have no comment at this time.

DR. BOYAN: And Dr. Holeman?

DR. HOLEMAN: I think the only thing that I wanted to ask about at this time has to do with the age of the patient. I know that one of your patients was age 91, and to what extent do you consider age to be a factor in the indication for use. I notice that your labeling speaks to mental, physical, psychological condition of the patient but it just seems to me that with a patient being 91 or older, and with the possibility of repeated surgery or repeated

invasive technique due to failure of the device that that somehow affects the quality of life of the patient at that age. Could you address that?

DR. WILSON: Well, I think that in terms of the indications for use of this device one of the indications or relative indications is advanced age, but that clearly needs to be evaluated carefully by the surgeon, and I think this falls into surgeon judgment. There are some patients that were included in this study where this device was used where the primary indication was advanced age.

Our feeling in that regard is that many times patients who are older have more difficulty understanding and following dislocation precautions. As Dr. Nelson will attest, the compliance of the patient is crucial in terms of providing long-term stability for anyone with a total hip.

Also, sometimes patients who are older may be quite a bit less active. Some of these patients are very minimal ambulators, spend much of their time sitting, even much of their time in a wheelchair and, therefore, are at increased risk for posterior dislocation.

The few patients in my study, a group of 61 that were older like that, were only undertaken really for unique and extreme circumstances. The one patient who at follow up was 96 actually had an old cemented all polyethylene cup

that was known to be loose for many years but was minimally symptomatic. Then she had a fall and she dislocated the cup with the cement attached to it from her acetabulum. We had no choice but to reoperate on her. And because she was somewhat demented and quite elderly, and going to be spending most of her time sitting, we elected to use this cup.

So certainly you have to look at the patient and what their ability to understand posterior distal dislocations precautions are, and look at their life style. Some people who are 88 or 90 are still relatively active and you can probably use just a standard cup on them. But it is the judgment of the surgeon, and I think that is where the surgeon needs to be very careful in doing that because, you are right, if they do dislocate one of these constrained cups then they need another operation and, obviously, that is a serious drawback.

DR. HOLEMAN: And the other thing I wanted to comment on, I think it was in your document somewhere that you indicated that the chances for failure decreased with an increase in surgeon implant, or the number of that -- maybe I am getting this wrong. Based on the number of times a surgeon has had an opportunity to place one of these devices, that the failure rate would decrease based on that.

DR. WILSON: That was not in my paper.

DR. BOYAN: Dr. Nightingale?

DR. NIGHTINGALE: That is actually a citation from the literature, and that is in my review packet that you got.

DR. HOLEMAN: Okay.

DR. NIGHTINGALE: That is not specific for this device. That is simply one of the things that is stated in standard textbooks as a factor.

DR. HOLEMAN: Okay.

DR. BOYAN: I have one comment that I would like to make. In all of the indications for use you have focused really on low mobility patients, relatively elderly people, people that have deficiencies that would cause them to become relatively immobile, and there is a large amount of ultra-high molecular weight polyethylene in this particular device. As you start moving towards younger and younger patients, which would be the case now as compared to when you initially put this device on the market, there is going to be greater chance for wear, and I just would like to caution you to consider that in your future approach to the design problem.

I want to give everybody a chance to get any more comments in. Dr. Skinner and then Keith, maybe you want to revisit something? Dr. Skinner?

DR. SKINNER: Yes, I wanted t o revisit two issues. One was yesterday I pointed out that for all the total hips I have done, I don't think I have ever seen a package insert. I would like to suggest that a package insert be put in a surgical technique manual, where it could be seen by the surgeon before the procedure.

The second is this problem with the cup fixation. Acknowledging, as my colleagues here have already done, that surgeons are technicians more than cognitians --

(Laughter)

-- perhaps the average orthopedic surgeon doesn't understand this step increase in difficulty in removing the cup, and particularly in use of the Arthopor cup where it is cemented in place. How is this information transmitted to the surgeon so that if an Arthopor cup is cemented in place it is going to provide the appropriate step increase in difficulty in removing it, since I doubt that the cement will provide a whole lot of tensile capability?

MR. OCHOA: There are two things that go to that. The Arthopor originally was cleared for cemented use and subsequently, I believe, got classified before the

acquisition for cementless use. But the key unit in all of this is, regardless of whether it is cemented or cementless, the indication of using screws instead of the locking pins to put the cup in there. So even if it was cemented, you still have the very end of flange where you can put peripheral screws, and those screws are still indicated so that resistance to tension would come from two, three or four, however many screws you are going to be putting on the cup.

And to your point, as we look at new generation design of cups or even improvements, that is the kind of balance that we need to strike regardless of the compressive resistance. Those screws would give you tensile pull-out strength, significant tensile pull-out strength depending on bone quality.

DR. BOYAN: Thank you. Dr. Markolf, is there anything you want to revisit?

DR. MARKOLF: No.

DR. BOYAN: Okay. Are there any other questions that the Panel would like to raise with members of the company or the FDA?

Hearing no further discussion, I would like to entertain a motion. I have to turn it back over to Jodi, who is going to give us instructions.

MS. NASHMAN: We have the FDA questions that we would like you to have discussion on.

DR. BOYAN: Oh, I am sorry, you are right. You are absolutely right. We have the FDA questions. Okay.

We have had several questions that they would like us to consider. I think we have overheads that we can have up again. We will review these questions as we go through. Each member of the Panel will have an opportunity to respond to each question.

The first question is, is the following proposed indication for use supported by the PMA information for the subject device? The S-ROM Poly-Dial Constrained Liner is indicated for use as a component of a total hip prosthesis in primary or revision patients at high risk of hip dislocation due to a history of prior dislocation, bone loss, joint laxity or intraoperative instability.

Why don't we begin with Dr. Holeman an d have her comment as she would like on this particular question?

DR. HOLEMAN: I think based on the indication as you have just read, I would say that the data support that indication. However, I did have a question prior to seeing the indication that you just finished reading because the indication that they initially supplied in their document indicated that it was indicated for use in patients

suffering with severe pain. And I think based on the literature that they supplied that it did not indicate -- the data did not indicate that it significantly relieved pain. As a matter of fact, I think they show that there were poor results based on the measure they used.

DR. BOYAN: Dr. Silkaitis?

DR. SILKAITIS: Based upon the information provided and the limited use of the product, the indication seems appropriate.

DR. BOYAN: Dr. Nelson? Roger?

DR. ROGER NELSON: Yes, no additional. It is based on the information provided.

DR. MARKOLF: I agree.

DR. BOYAN: Let the record reflect that Dr. Markolf agrees. Dr. David Nelson?

DR. DAVID NELSON: Yes.

DR. BOYAN: He also agrees. And now Dr. Besser?

DR. BESSER: I agree.

DR. BOYAN: Dr. Rangaswamy?

DR. RANGASWAMY: I agree.

DR. BOYAN: Dr. Rudicel?

DR. RUDICEL: I agree.

DR. BOYAN: Dr. Greenwald?

DR. GREENWALD: I agree.

DR. BOYAN: Dr. Skinner?

DR. SKINNER: Actually, I don't agree.

DR. BOYAN: Would you expand on that please?

DR. SKINNER: Well, since the wording is such that it says, "in cases such as previous" etc., I think that it is acceptable wording because it doesn't preclude other things but I think it might be more accurate to include neuromuscular disorders and I think deficiency of surrounding musculature would probably be a better way of putting it because palsy indicates that it is a nerve problem more than a muscular problem, and frequently it is a muscular problem that is the deficiency abductor musculature that keeps these from staying in. So I would suggest those two changes.

I don't think that pain is necessarily an indication for this operation. I think that patients have significant anxiety that they are going to have a dislocation and that, by itself, is an adequate indication.

DR. BOYAN: Thank you. Any other comments? Let's go to the next series of questions. What are the appropriate contraindications, warnings and precautions for the device? And I am going to do these as a set. Should the indications be limited in any way? Should there be limitations on the

usage of the device for certain patient populations? Let's begin with Dr. Markolf.

DR. MARKOLF: I would probably let the clinicians speak to that.

DR. BOYAN: Dr. David Nelson?

DR. DAVID NELSON: I think that is fine. I would just echo something that we did bring up yesterday and that Dr. Skinner mentioned again, that the surgeons don't have access to the product insert until it is too late. So if that kind of information is in the surgical technique manual, that is very helpful to us.

And we probably need to put some sort of red flag on the single-use only because you are using a different sense and possibly a different phraseology should be used.

Other than that, I have no objection.

DR. BOYAN: Dr. Besser?

DR. BESSER: I have no comments.

DR. BOYAN: Dr. Rangaswamy?

DR. RANGASWAMY: I think it has already been said in the first question, and Dr. Skinner added to it.

DR. BOYAN: Dr. Rudicel?

DR. RUDICEL: I have nothing further to add.

DR. BOYAN: Dr. Greenwald?

DR. GREENWALD: Nothing further.

DR. BOYAN: And Dr. Skinner?

DR. SKINNER: Nothing further to add.

DR. BOYAN: Dr. Holeman?

DR. HOLEMAN: Nothing further to add.

DR. BOYAN: Dr. Silkaitis?

DR. SILKAITIS: Nothing further to add.

DR. BOYAN: And Dr. Roger Nelson?

DR. ROGER NELSON: Nothing further to add.

DR. BOYAN: I might like to have there be some statement made about consideration of the activity of the patient; that there not just be a positive statement that the indication be low mobility or low activity patients, but there might be a contraindication or at least a concern that a high activity patient might not be the right patient for this device.

And I think we also had in the discussion several comments made about being clear to the surgeon that the ring and the insert go together as a team.

DR. SKINNER: Dr. Boyan, could I comment on that?

DR. BOYAN: Yes.

DR. SKINNER: I don't understand the reason for limiting it to low activity patients.

DR. BOYAN: I don't want to limit it. I was trying not to state that. I was just trying to bring to the surgeon's attention that they consider that --

DR. SKINNER: Yes, it should not be a --

DR. BOYAN: Limitation.

DR. SKINNER: -- a limitation based on activity.

DR. BOYAN: Definitely not a limitation. I didn't mean to imply that it was a limitation. Okay, any other comments on this?

Okay, question three, based on the data derived from the clinical studies or other sources of adequate scientific evidence for the S-ROM Poly-Dial Constrained Liner, are specific clinical evaluations or tests needed for the selection of patients for the device?

We will begin this time with Dr. Rudicel.

DR. RUDICEL: I don't think any further evaluations than have been done.

DR. BOYAN: Okay, we can quickly around. Dr. Greenwald?

DR. GREENWALD: I think the ordinary clinical indications or a dislocated hip are probably more than sufficient.

(Laughter)

DR. BOYAN: Dr. Skinner, anything to add?

DR. SKINNER: Nothing to add.

DR. BOYAN: Okay, coming around, Dr. Holeman?

DR. HOLEMAN: Nothing to add.

DR. BOYAN: Dr. Silkaitis?

DR. SILKAITIS: Nothing to add.

DR. BOYAN: Dr. Roger Nelson?

DR. ROGER NELSON: Nothing to add.

DR. BOYAN: Dr. Markolf?

DR. MARKOLF: Nothing to add.

DR. BOYAN: And Dr. David Nelson?

DR. DAVID NELSON: Nothing to add.

DR. BOYAN: Dr. Besser?

DR. BESSER: Nothing to add.

DR. BOYAN: And Dr. Rangaswamy?

DR. RANGASWAMY: Nothing to add.

DR. BOYAN: All right. The next set of questions, because of the constrained design of this device, should there be any special instructions for the short- and long-term patient management, including activity restrictions? Should any additional or special instructions be added to the surgical technique for total hip arthroplasty when using the S-ROM Poly-Dial Constrained Liner? And why don't we start with you, Dr. Skinner?

DR. SKINNER: I think that I have already addressed several of the issues I think that are important to go into the surgical technique. I think that the orientation of the metal ring is extremely important here. I don't think that many surgeons understand that it has two directions because they don't read the insert. The representative from the company present at the time of surgery may not make that totally clear, and the surgeon may not even listen.

(Laughter)

But I think that -- well, I will just say that the other things I have said should be mentioned regarding fixation of the cup, and so forth, second use and so forth.

DR. BOYAN: Okay, I don't want you to think that I am going to always go in the same direction. You are next, Dr. Greenwald.

DR. GREENWALD: Thank you. I just want to pick up on Dr. Skinner's point. You know, maybe there is some reality to an arrow that says "this end up" because I will bet you dollars to doughnuts that some of the ring dislocations have occurred probably because they were put in backwards. It is probably a very easy mistake to make.

The second point, and I think this is really important and Dr. Markolf brought this out, you know, this

constrained poly-dial cup should be used in conjunction with screws and not the lugs or pegs they talked about, which is a multi-factor in the non-constrained S-ROM designs. I think that is really important for clarity and that should be part and parcel of the surgical technique.

DR. BOYAN: Dr. Rudicel?

DR. RUDICEL: I have nothing more to add.

DR. BOYAN: Dr. Rangaswamy?

DR. RANGASWAMY: I have nothing to add.

DR. BOYAN: Dr. Besser?

DR. BESSER: I have one comment on the surgical procedure manual. Page 11 of the manual talks about assembly of the constrained socket in situ, and talks about practicing, but on item 7 there it does state, "ensure that the inside of the reinforcing ring and the mating shoulder of the socket are clean" etc., etc., and it does mention the orientation of the ring, but then talks about practices heavily with demo socket; use edge of knife blade to remove reinforcing ring from the shoulder, which I am assuming here is instructions for practicing with the demo socket, but because it is in this manual surgeons might believe that if they put it on backwards using an edge of a knife they can take it off, turn it around and put it on frontwards. And nowhere in here does it boldly say don't do this in real

surgery; only do this in practice. Rewording of this instruction is recommended.

DR. BOYAN: Thank you, Dr. Besser. Dr. David Nelson?

DR. DAVID NELSON: Nothing to add, other than I know that the FDA team will be dealing with these issues as they come to their final conclusions on that, and it is interesting, Mr. Noiles was thinking some of that was funny. As a surgeon, I think these things happen all the time and we need to make it very simple. I am also an engineer. As an engineer, we try to design things so you can't do it wrong. I have nothing more to add.

DR. BOYAN: Thank you. Dr. Roger Nelson?

DR. ROGER NELSON: I would just add that I would assume that the physician or the surgeon would adequately communicate the type of prosthesis to the referring physical therapist or other care-giver so that they would know the limitations of motion etc. So that would be my only concern, that the type of prosthesis would be so noted.

DR. BOYAN: Thank you. Dr. Silkaitis?

DR. SILKAITIS: Nothing further to add.

DR. BOYAN: And Dr. Holeman?

DR. HOLEMAN: I do feel that some information should be provided, some instruction on the patient

management, including activity and restriction, but I think that can best be addressed under question number four.

DR. BOYAN: Thank you. Now, the final question that is being asked of us is, is a separate patient information sheet necessary for the S-ROM Poly-Dial Constrained Liner? If so, what types of information should be contained in a patient information sheet? And, Dr. Holeman, why don't you begin this one?

DR. HOLEMAN: Okay, I do feel that for the benefit of the patient that a separate patient information sheet should be provided, and I am not sure whether that should be in the package or should that information just be made available to the patient. A patient has a right to know about the device, the use of the device; what kinds of problems can be encountered in the use of the device; what long-term complications may develop. And I think this should be written in terms that a patient can understand, in lay terms and not necessarily medical terms that would often be communicated to the patient by physicians.

DR. BOYAN: Thank you. Dr. Silkaitis?

DR. SILKAITIS: In terms of a patient information sheet, sometimes that is very difficult to come up with because there is the doctor-patient relationship. I do agree that patients need to know about the treatment that they are

getting and probably that is sometimes best served by that patient-doctor relationship. Probably if the component or the product that is being used is truly novel or unique and there are some risks that are unknown to the general surgeon population, maybe that is where it is more appropriate.

DR. BOYAN: Thank you. Dr. Nelson? Roger?

DR. ROGER NELSON: I also agree with a patient information sheet. I believe that it has been fairly well illustrated, especially in the low back literature, when they had developed at the Agency for Health Care Policy and Research a patient sheet, that the compliance, the treatment and compliance with the care went up dramatically. So some kind of mechanism.

Also, you walk the tightrope of this issue that we talked about yesterday of having an iatrogenic effect too of the patient information sheet. So, I mean, t here has to be a balance here of the issue. But the patient should be aware of what they have, and what some of the issues are that should be identified.

DR. BOYAN: Thank you. Dr. Markolf?

DR. MARKOLF: I don't see any expressed need for an information sheet. I think the communication between the doctor and the patient -- they will probably be more apt to

listen to their doctor than read a sheet. Maybe not. I don't know.

DR. BOYAN: Dr. David Nelson?

DR. DAVID NELSON: Nothing to add.

DR. BOYAN: And as a personal patient, I would like to state that the patient information sheet is very important to the patient. Dr. Besser?

DR. BESSER: I hate to disagree with Dr. Markolf, but eventually the patient goes home and then the doctor is not there to ask the question. I think a patient information sheet is worthwhile.

DR. BOYAN: Dr. Rangaswamy?

DR. RANGASWAMY: Certainly, a patient information sheet is important, but if the physician or the surgeon doesn't talk to the patient and explain what is being done it doesn't matter how many sheets of paper you give. I think it is useful to take something home but what the patient is really going to remember is the rapport they have with the doctor and how they can deal with that.

DR. BOYAN: Dr. Rudicel?

DR. RUDICEL: I agree that the doctor-patient relationship is most important and conveys information, and a sheet that has -- that I would say is rather brief can be

helpful for the patient to just look at when they are away from the doctor.

DR. BOYAN: Dr. Greenwald?

DR. GREENWALD: Well, I don't put the fly in the ointment here or the cat amongst the pigeons, but I think there is -- not being a surgeon but very appreciative of the relationship between a doctor and a patient, it is called informed consent, and I think it is obligatory on the physician's part, the surgeon's part to inform the patient, and maybe this little check list in simple English might be given to the patient. But then, as my esteemed colleague on my right just pointed out, what happens if you get in there and you find out that, oh my goodness, we are not going to use a poly-dial constrained hip; we can do this by just, you know, trochanteric advancement or some other soft issue reconstructive process which just may save the patient the use of the revision cup? Then what? The cat is out of the bag and the doctor then has to go back and re-explain to the patient why he or she didn't perform the surgery they anticipated.

DR. BOYAN: Dr. Skinner?

DR. SKINNER: Thank you, Dr. Boyan. I disagree with Dr. Boyan. I think that a patient information sheet provided before surgery interferes with the informed consent

process, and I think that providing a specific one for a constrained liner significantly ties the surgeon's hands and obligates him to a given procedure, and takes away the latitude to do the best thing for the patient. I wouldn't be against having one as a post hoc, after the surgery information sheet but I think that requiring one to go to the patient before surgery is definitely a bad idea. I think that we've got to be careful about this information sheet business because, you know, when you go to do a cemented total hip and you use a cement restrictor you need an information sheet for the cement restrictor. Then do you need one for the bone cement because there are six different kinds of bone cement on the market? Do you need one for the hip prosthesis? Do you need one for whether you are going to use a chromium cobalt head? And then do you need one for whether you cement it? Fourteen information sheets later the patient is walking out of there, and if it is before surgery, then you are caught. You are obligated as to what you have to do. I disagree with patient information sheets preoperatively.

DR. BOYAN: Okay, first Dr. Roger Nelson, then me, then Sally Rudicel, Dr. Rudicel.

DR. ROGER NELSON: I did not take into account that this would be pre-surgery. My assumption would be that

there would be some simple take-home device that the patient would have that would look at describing these issues. Again, it would be a very simple kind of device because, having worked with a number of surgeons through the past 30 years, I have found that they don't often spend a lot of time with the patient and that the physical therapist ends up spending a good deal of time with the patient, and such. So when they have questions, the patient can bring in that sheet of paper and say what do they mean by this, and this kind of issue. But I certainly didn't mean a preoperative kind of sheet.

DR. BOYAN: I think we have clearly hit on something that is very important, and I would like to encourage the FDA to consider having possibly a separate panel discussion on some of these issues on patient information. It is really independent of this particular product that is under discussion right now. This is clearly a much, much bigger issue as to how much information is appropriate, and there are certainly legal issues involved that are beyond the scope of this discussion. So that would be my recommendation as to the patient sheet, that it be a separate topic on its own and be discussed in full entirety with ethics, legality, patient concerns, surgeon concerns all brought forward. Dr. Rudicel?

DR. RUDICEL: As one of the practicing surgeons on the Panel, I wanted to concur with what Dr. Skinner said, and in making my previous comments I was also under the assumption that this would be a postoperative patient information sheet. I think patients need as much information as is necessary but I don't in any way want to restrict what the surgeon can do in the operating room.

DR. BOYAN: Right. We have Dr. Holeman, D r. Nelson and then Dr. Rangaswamy.

DR. HOLEMAN: Okay, I just want to comment and reinforce what Dr. Boyan has said in reference to the need for an information sheet, and this is not to say that the information sheet should be that procedural oriented, but that the patient should have information. And having been at the bedside with physicians when they provide information to patients, I do know that once the physician leaves the room nurses are summoned back to the room to help explain what is going to happen to the patient in surgery. So I just don't think that this should be minimized; that we are living in an information age and, as far as restricting information, I think the physician has a right to decide what amount of information she or he wants to give the patient. But as far as what the patient can or cannot have in the line of that, I just don't think that that decision should be made to do

that. And I agree with Dr. Boyan that this should be discussed because when you think in terms of limiting information there is a bigger issue.

DR. BOYAN: We are going to get into a philosophical issue that is not appropriate to the discussion at hand because the discussion at hand is a particular product and we need to deal with the product and then move to the next step, and I think make a recommendation to FDA that we deal with the other issue, which is a much bigger issue that is independent of this product. Yes, Dr. Nelson, stick right to the issue of the product, if you could, please.

DR. DAVID NELSON: I will skip the question then.

DR. BOYAN: Okay. How about you, Dr. Rangaswamy?

DR. RANGASWAMY: I will stick to the issue here that we are talking about. We are talking about patient information and the question, I think, that is being mixed up here is are you going to provide details about the device itself to the patient, which is a whole different issue when you are talking about patient information? The rest of it that everybody is bringing up is really between the doctor and the patient. So I think we need to really clarify that. You can certainly write all you want about the device and give it to the patient but I think that is where we were

coming from. I am a practicing orthopedic surgeon too and I think that let's not mix up the discussion about the operation and why it is being done and what the pros and cons are with the patient information in terms of the product. So that is where I think that that kind of patient information sheet for the product is meaningless to the patient. The rest of it, yes, it has to be a doctor-patient relationship. So I don't think we should mix that up.

DR. BOYAN: Okay. Dr. Skinner, do you have a comment directed to the product?

DR. SKINNER: I agree.

DR. BOYAN: Dr. Rangaswamy covered it? Okay. Then is there any further discussion on any of these questions? I would like to ask Dr. Witten if we have addressed the concerns of the FDA.

DR. WITTEN: Yes, thank you.

DR. BOYAN: Then let us now turn it over to Ms. Nashman, who is going to explain to us what the mechanics are for the voting process.

MS. NASHMAN: This is a mechanical engineering class? The mechanics of voting are as follows: Now that you all have finished your discussion, you are going to be asked formally to vote on a recommendation to FDA for this submission. Dr. Boyan will ask for a motion from the Panel.

And there are three options for panel recommendations to the FDA. Those are approvable; approvable with conditions; or not approvable. And they are described as follows: If you believe that the PMA is approvable you are saying that the FDA should approve the PMA with no conditions attached.

If you vote for a recommendation of approvable with conditions, you are attaching specific conditions to your recommendation that FDA approve the PMA. The conditions must be specified when the motion for approvable with conditions is made. In other words, you may not vote for approvable with conditions and then determine the conditions later or not describe the conditions at all. Examples of pre-approval conditions of approval are changes in draft labeling and resolution of questions concerning the submission or the device just previously discussed. Examples of post-approval conditions are postmarket studies and the submission of periodic reports. In all cases you should propose the extent of the conditions of approvability, such as the number of patients to be followed and/or the number, interval and type of reports to be considered. In all cases you must state the reason or the purpose for the condition.

The third option is a recommendation of non-approval. The Act, Section 515(b) Part 2, paragraphs A

through E state that a PMA can be denied approval for a number of reasons. I will discuss three relevant reasons.

The first is a lack of showing of reasonable assurance that the device is safe under conditions of use prescribed, recommended or suggested in the labeling. In this case, safe means there is a reasonable assurance that the device is safe when it can be determined safe based upon valid scientific evidence that the probable benefits to health from the use of the device, when accompanied by adequate directions and warnings against unsafe use, outweigh the probable risks. It is a benefit to risk ratio. The valid scientific evidence used to determine the safety of a device must adequately demonstrate the absence of unreasonable risk of illness of injury associated with the use of the device for its intended uses and conditions of use.

A second reason to suggest disapproval is lack of showing of reasonable assurance that a device is effective under the conditions of use prescribed, recommended or suggested in the labeling. Effectiveness can be defined as a reasonable assurance that a device is effective when it can be determined that it will provide clinically significant results. This determination must be based upon valid

scientific evidence that a significant portion of the target population will provide clinically significant results.

Finally, the PMA can be recommended for non-approval if based upon a fair evaluation of all the material facts and your discussions you believe the proposed labeling to be false or misleading.

If you vote for disapproval, FDA asks that you identify the measures that you believe are necessary or the steps that should be taken to place the application in an approvable form. This may include specifics on additional studies.

The voting process begins with a motion from a member of the Panel, and it may be for any of the three options just described: recommendation for approval, approvable with conditions, or disapproval. If the motion is seconded, the Chair will ask if anyone would like to discuss the motion, and so on. Please remember that the proceedings are taped for later transcription. Non-verbal signals are not captured on tape. If you wish to second, you should state so rather than nodding your head or waving your hand. You may vote yes, no or abstain. The majority vote carries the motion and the voting members for this morning's portion of the meeting are as follows: Drs. Besser, Greenwald and Markolf, D. Nelson, R. Nelson, Rangaswamy, Rudicel and

Skinner. Dr. Boyan, as the chairperson, votes only in the case of a tie. Dr. Boyan?

DR. BOYAN: Thank you. Before beginning the voting process I would like to mention for both the Panel's benefit and for the record that the votes taken are votes in favor of or votes against the motion made by the Panel. Votes are not for or against the product. Do I hear a motion? Dr. Greenwald?

DR. GREENWALD: Dr. Boyan, I would like to make a recommendation that the PMA P960054, Poly-Dial Constrained Liner, be found approvable with conditions. And I would offer the following conditions based on what I think is a fairly thorough discussion of the issues in hand.

The first condition is that -- the admonition, in fact, insert labels are seldom read by the practicing surgeon, that, indeed, some measure be made by the company to insert sufficient information such as appropriate assembly instructions so there is no doubt as to which way the components are assembled, and other such information particular to the use of screws in the use of this particular device, and references to pegs be deleted and only utilized with the non-constrained liners that the company markets.

I also would like to suggest as part of that information that since these are not all that frequently produced surgeries but do occur, that perhaps a video or some visual means of information might be supportive to the practicing surgeon.

The second condition that I would like to offer as a suggestion to the corporation is that as time goes by the benefits of what seemed to be a reasonably long-term success rate, getting out to ten years of stability and non-dislocation afforded by these devices, be reinforced by some additional laboratory testing, which is not conditional on approval but in their own best interests and the interests of patient longevity, that they consider conducting more dynamic tests of the polyethylene femoral head shell assembly where, indeed, after a period of time dislocation via impingement be gotten so that some measure of anticipated failure be gleaned. Since not only is there a whole class of patients other than chronically ill, and aged, and demented which dislocate their hips and they may be in the younger age range, more active category, and I think this is probably in the best interests of all, patients and company. That is my recommendation, Madam Chairman.

DR. BOYAN: Thank you very much, Dr. Greenwald. Do I have a second for this motion?

DR. DAVID NELSON: Before we second, may I ask a question of Dr. Greenwald?

DR. BOYAN: Yes, I will allow that. Is this a clarification of the motion?

DR. DAVID NELSON: Yes.

DR. BOYAN: Okay.

DR. DAVID NELSON: You said, Dr. Greenwald, that the second is really not dependent on the approval. So is it really appropriate to have that as part of the motion? Am I correct in saying that is just some advice that we would like to give the company but it is not part of the motion proper?

DR. BOYAN: I think some of that is in the motion proper and should remain.

DR. GREENWALD: I think that I don't consider that to be a mandate of approval but I do consider it to be important because, you know, as I indicated earlier, I wouldn't like to see this device be the victim of its own success. We are going to get beyond eight years in clinical utilization of this device, and I am simply suggesting that polyethylene, as Dr. Boyan has already pointed out, does

wear and in time all devices, particularly if they outlive their patients, can get into difficulty.

DR. DAVID NELSON: Thank you. I will second.

DR. BOYAN: Okay, so we have a second by Dr. David Nelson. Now the motion is open for discussion. Is there any discussion of the motion? Yes, Dr. Besser?

DR. BESSER: As to the changes in the labeling and paper that goes with this, I would like to specifically point out the instructions for the placement of the ring and ask that the company emphasize that there is no re-use once the ring is snapped in place. If it is removed the liner and the ring should be discarded and another should be used. And I might suggest separating out parts of their surgical procedure manual for the constrained versus the semi-constrained prosthesis, again, with the issue of the screws versus pins.

DR. BOYAN: The screws versus pins is in the original motion.

DR. BESSER: Yes. I would like to see a separate surgical procedure manual, I guess, or some changes to the surgical procedure manual made such that in the portions where they describe that this can be attached with screws versus pins, possibly put a parenthetical statement, stating

if using a constrained liner pins may not be used; screws must be used.

DR. BOYAN: Okay. Is there an objection to that amendment? And the other amendment that the ring be used always with the liner, that they be used as a unit?

DR. BESSER: The comment about the single-use --

DR. GREENWALD: You are quite correct. I guess I want to add a third comment to my motion, Madam Chairman, and that is, it should be clearly stated in the surgical instructions as well as probably the package insert that this liner and ring are a one-time assembly -- clearly stated so that there is no ambiguity of intent on the part of the implanting surgeon that, indeed, if it is assembled once and then removed, disassociated, a new system should be utilized.

DR. BOYAN: Okay. And Dr. Markolf, do you have anything that you want to modify the motion?

DR. MARKOLF: I would like the motion discussed.

DR. BOYAN: Okay. So we are throug h modifying right now and now we are discussing again. Let me just make sure the seconder accepts the modifications.

DR. DAVID NELSON: Yes.

DR. BOYAN: Okay. All right, go ahead.

DR. MARKOLF: I would also like to emphasize additional testing and I will tell you why. First of all, I think it is time, you know, since things were lost in the fire. It wouldn't be too much additional work to do that testing and get some lever-out moments in the impingement mode. But, secondly, I think once you have a number and as you come down the road and your device is compared to other devices, as I think we will hear about this afternoon -- I guess we can't talk about that yet because it is not public record.

DR. BOYAN: Right.

DR. MARKOLF: But when other devices do become available and bend-out moments for those are known, you can compare your device to those and perhaps, you know, in the field you can hone in on what would be a more appropriate capture moment because, you know, this device did have quite a few that snapped out, and that may not be the case with some other devices. So I think numbers on these are very valuable and I would like to strongly recommend that you do additional testing.

DR. BOYAN: Okay. Dr. Rudicel?

DR. RUDICEL: I would still like to clarify the second part of the amendments here. I personally don't think

that our vote should be contingent upon further testing. I think it is an excellent suggestion --

DR. MARKOLF: These are suggestions.

DR. RUDICEL: -- but I want to be clear, in terms of how I am going to vote, if this is a suggestion only.

DR. MARKOLF: It is a suggestion only.

DR. GREENWALD: That was intended in my condition too, a suggested mechanism --

DR. BOYAN: So the second part of this motion, the original second part was that -- I took it to be a suggestion also, the idea that there be additional testing so that they could develop an anticipated failure mode for more active patients, and everybody seems to be comfortable with that being a suggestion and not part of the conditions for approval. Am I correct on that? Okay, Dr. Rangaswamy?

DR. RANGASWAMY: Dr. Greenwald had said about the video being given. I just want to, I guess, interject a note of caution. The question is are we now overstepping in terms of looking at the training of surgeons, and what the Academy does in terms of what residency programs and fellowships are supposed to do. You know, where is the role of the company? We hope sincerely that practicing orthopedic surgeons are being trained, and the untrained surgeon isn't going to go and do one of these difficult revision total hips. We

sincerely hope that. So it always bothers me. I mean, I think it is nice to have it available but it can't be an ideal thing. You should either take away the license of the people --

DR. BOYAN: Dr. Rangaswamy, why don't you let me restate the motion, and I will state it so vaguely that it will leave it open --

(Laughter)

-- to the FDA to determine how they want to handle it.

DR. GREENWALD: Excuse me, I did mean that again as a suggestion. I mean, it is common practice for champion users or, you know, prolific users of a device to make surgical techniques and operative procedure part and parcel of the availability of a device.

DR. BOYAN: Would you not agree, Dr. Greenwald, though our goal here is to get a greater degree of information to the surgeon as to how he or she should use the device?

DR. GREENWALD: I totally agree.

DR. BOYAN: So the specifics of how that is accomplished doesn't have to be our concern. We have given them lots of advice on how to do it.

DR. GREENWALD: And that is what this was intended as.

DR. BOYAN: Okay. So let me restate the motion. The motion is that we recommend approval with the conditions that the -- I have to read my handwriting -- that the insert labels include information to ensure that the process for assembly is clear; that the use of screws be clearly stated, that that is preferable and, in fact, to the consideration of a separate surgical procedure manual or section that clearly states that for constrained devices screws be used and that that not necessarily be the case for unconstrained devices; that there be consideration given to more information being supplied to the surgeon as to how these devices should be used and when they should be used; and that there be a clear statement that the device is a one-time assembly; that the ring and the liner are a unit and that they should not be used separately; and, finally, that a recommendation be made that the company consider additional testing in the future to develop an anticipated failure mode that might be of value to predicting how this should be used in more active patients.

That is the motion plus our suggestions --

DR. BESSER: Excuse me, one clarification, for this device the use of screws is not preferred; it is required.

DR. BOYAN: The use of screws is required. Clearly state that the use of screws is required, and that it be clearly stated in the manual and any information provided to the surgeon as to how the device should be used and that they understand that it is to be used with screws. Okay? Let's vote. All in favor of the motion, raise your hand. We are on tape. We actually have to state each person's vote.

DR. SKINNER: Harry Skinner, approved.

DR. GREENWALD: Seth Greenwald, approved.

DR. RUDICEL: Sally Rudicel, approved.

DR. RANGASWAMY: Leela Rangaswamy, approved.

DR. BESSER: Marcus Besser, approved.

DR. DAVID NELSON: David Nelson, approved.

DR. MARKOLF: Keith Markolf, approved.

DR. ROGER NELSON: Roger Nelson, approved.

DR. BOYAN: Thank you.

DR. WITTEN: Excuse me, I would just like to clarify that when people were voting for approved meant approved with the conditions as stated.

DR. BOYAN: Absolutely true, with conditions as stated.

DR. WITTEN: Maybe you could go around and have everyone clarify that and also give their reasons for recommending approval with conditions.

DR. BOYAN: Okay. Let's just go ahead and start with you, Dr. Skinner.

DR. SKINNER: Based on the scient ific information provided by the company and by the FDA, I feel that this meets the qualifications for approval with the conditions stated in the motion.

DR. GREENWALD: I too believe that valid scientific evidence has been presented, and I also believe that the company has demonstrated efficacy in the presentation of their data, as has the FDA in their investigation and assessment of it, and I believe that it is important to make these devices available both to the surgeon and the patients they serve for this disabling conditions. So I agree with the motion with the conditions stated.

DR. BOYAN: Dr. Rudicel?

DR. RUDICEL: I think both the company and the FDA have shown that this device is safe and efficacious, and I vote for approval with the conditions so stated.

DR. BOYAN: Dr. Rangaswamy?

DR. RANGASWAMY: I agree with everything that has been said, and approve the motion with the conditions that have been stated.

DR. BOYAN: Dr. Besser?

DR. BESSER: I agree with everything that has been said, and vote for approval of the motion with the conditions stated.

DR. BOYAN: Dr. David Nelson?

DR. DAVID NELSON: Yes, I do think there was valid scientific evidence that it is both safe and effective. So I voted for approval, and I thought that it was both in the company's best interests as well as the patients' best interests that we do have these conditions because it is very easy for slight things to go wrong, and I think with these conditions we heighten the safety and effectiveness of the device.

DR. BOYAN: Thank you. Dr. Markolf?

DR. MARKOLF: Yes, I think it is an important device that a surgeon have in his armamentarium, and I think it can do a lot of good for end-of-the-road patients. That is why I voted for approval.

DR. BOYAN: Dr. Roger Nelson?

DR. ROGER NELSON: I agree with all the previous statements and I approved with the conditions stated.

DR. BOYAN: Thank you, everybody. The session is adjourned.

MS. NASHMAN: We are going to resume at one o'clock.

(Whereupon, at 11:55 p.m., t he Panel adjourned for lunch, to reconvene in open session at 1:00 p.m.)

AFTERNOON SESSION

MS. NASHMAN: If we could all assemble, it is the last part of the Orthopaedics and Rehabilitation Devices Panel meeting. We are about to start and I will just turn the Panel over to Dr. Boyan.

DR. BOYAN: Welcome to this afternoon's session. Since our format seems to be working pretty well, we will start off the format this afternoon with, first, the presentation from Osteonics, followed by the presentation from the FDA, followed by the two reviewers from the Panel, and then we will open it up for discussion. So that will be the order of business.

I would like to remind the public observers at this meeting that while this portion of the meeting is open to public observation, public attendees may not participate, except at the specific request of the Panel.

We are now ready to begin with the sponsor's presentation. I would like to ask that each speaker state his or her name and affiliation to the firm before beginning the presentation. Osteonics?

Presentation by Robert A. Koch, J.D.

MR. KOCH: Good afternoon. Dr. Boyan, members of the Panel, representatives of the FDA, ladies and gentlemen,

my name is Robert Koch, and I am director of regulatory and legal affairs for Osteonics Corporation.

We are here this afternoon for your review of Osteonics' premarket approval application for the continued commercial marketing of the Osteonics Constrained Acetabular Insert.

Today, I will provide you with some background information regarding our device and what has brought us to today's meeting. I will be followed by Dr. Michael Manley, Osteonics chief scientific adviser, who will provide insight into the design of the device; its testing; its intended use and the marketing history for the product. Dr. Manley will also address the niche population for which this product is intended, and he will then detail the data from two clinical studies which address the subject device, as well as several case histories that provide valuable insight into the usage of the constrained insert. Dr. Manley will then conclude our presentation with a summary of its content.

Unfortunately, Dr. Andrew Glassman will not be able to join us today as he has been retained in emergency surgery, coincidentally using an Osteonics constrained acetabular insert.

(Laughter)

All right, after our presentation when questions and answers will begin, several other Osteonics employees will be available to assist addressing any of the Panel's questions.

Osteonics' PMA for its constrained acetabular insert was prepared and submitted in response to the FDA's call for PMAs on September 17, 1996, for Class III pre-amendment devices. The devices for which PMAs were called were believed to be in disuse. It was thought that the call would not force the removal from the market of devices which bear still a significant clinical need. However, as we have seen from the presentations yesterday and today, there are still some commercially available devices which do provide a significant clinical need, yet, are interpreted to fall within the targeted classifications and, thus, now require PMAs to remain on the market.

The last point is important to stress. The Osteonics constrained acetabular insert has been commercially marketed since April of 1989, at which time it was determined substantially equivalent in accordance with the FDA's 510(k) premarket notification process. Thus, your decision today will not be based on the traditional review of a product which is being introduced into commercial market for the first time subsequent to the performance of

an investigational device exemption study. Instead, the issue today is whether or not to remove a device from the market which has provided physicians with the ability to successfully treat some of their most difficult patients, those with, or prone to chronically dislocating hips.

The treatment alternative here is through a prosthetic device which offers the recipient a continued degree of hip function rather than fusion of the individual's hip. We urge the Panel to recognize this distinction in their deliberations.

The data which you will be reviewing, we believe, falls within the definition of valid scientific evidence. It meets the requirements which are seen on the right-hand side of the screen. It consists of well-documented case histories, as well as reports of significant human experience with the marketed device. We do not represent that it has been done under controlled studies or partially controlled studies. However, we do believe it does meet that definition.

As you heard earlier in the presentation, the Class III classification for this category of devices came about because of the clinical experience with the Sivash hip stem. It was due to the poor clinical results of this specific device that all constrained hips were placed into

Class III. However, the Osteonics constrained acetabular insert is very different from the Sivash hip. It does not have a hard linkage across the joint. It has assembly and reduction of the device which is the same as conventional hips. And the constrained insert can be revised as a unit without removing the entire joint.

We believe that today there is sufficient clinical experience with this contemporary constrained hip to clearly identify the niche population which benefits from the device. For patients receiving the Osteonics constrained insert more conservative treatment measures typically have already failed, and the only remaining alternative is hip fusion.

The benefits of our con strained hip clearly outweigh the potential risks. We believe that there is sufficient evidence to demonstrate Osteonics constrained acetabular insert offers a safe and effective alternative to hip fusion surgery.

At this time, I would like to turn the presentation over to Dr. Michael Manley.

Presentation by Michael Manley, Ph.D.

DR. MANLEY: Good afternoon. I am Michael Manley, chief scientific advisor to Osteonics. I would like to ask

my colleague here to change the slides for me. I can only concentrate on one thing at a time.

Let me just show you first the components of this device. It is very dissimilar from the Sivash hip that was shown on the previous slide. It has a number of major components. It has an outer polyethylene insert, which is at the top left of the slide on the right, and a retaining ring. You might like to note that the outer polyethylene insert fits into the acetabular shell with the same locking mechanism as do all of Osteonics inserts, both when this device was first designed and the inserts that are currently on the market.

The three components on the right of this slide make up a bipolar component which is identical to the commercially available bipolar components that the company did and still does have on the market. I would like to show you in a moment how all of these components come together.

All of the materials used in these devices meet ASTM standards, as you can see on these slides, as do the commercially available devices from which these are derived.

In function, t he bipolar is assembled by the company into the outer polyethylene insert. Intraoperatively, the outer polyethylene insert is assembled into the metal acetabular shell and the surgeon then puts

the femoral head into the bipolar. There is no locking mechanism for the surgeon to actually implant. The locking mechanism, the mechanism which retains the bipolar in the polyethylene insert is a factory-installed locking ring.

Once assembled, the articulation occurs both at the head to bipolar interface and at the bipolar to the insert interface. So there is no preferable area of motion on this component. The motion can occur at either interface.

I have in my hands actually one of these components. This is the constrained insert. It has this outer plastic shell I showed on the section view, and trapped within it is this bipolar component. This is assembled into the already implanted metal acetabular shell. Then the surgeon simply snaps the head of the femoral stem inside the bipolar, like that.

If he wishes to remove this component, disassemble these components at any time, he simply does so with this key. This is an identical key as used in Osteonics bipolar which is used in hemiarthroplasty. If you like, at the end of this talk I can pass these components around to you.

All of these components have undergone the standard non-clinical laboratory studies, such as bioburden, cytotoxicity and biocompatibility, and they have also

undergone shelf-life studies to prove that they are sterile at a minimum of five years on the shelf.

At the time that the original 510(k) on this device was submitted, mechanical testing was done, and I would like to quickly run through that with you.

The first test that was conducted, back in October of 1988, was one of these components was assembled into its shell. The shell was placed at 45 degrees to the load axis in a testing machine. A femoral head with a 22 mm bearing was assembled into the bipolar and then a compression-compression fatigue load from 100 to 1500 lbs. at a frequency of 20 Hz was applied to the construct.

It was found at that time there was no failure of this insert, no failure of the locking ring, no failure of the bipolar, and at the end of the test the device seemed to be completely intact.

The other mechanical testing that was done was so-called cam-out tests, also done in October of 1988, and the reason these cam-out tests were performed is that it was determined that the distraction type of tests where the head is pulled out of the implant has little clinical relevance, and the real relevance is can this implant be made to dislocate if neck impingement occurs once the surgeon has placed the component?

So in this test the stem was assembled to the constrained insert into the shell. The stem was then rotated to full abduction until neck impingement occurred on the edge of the constrained insert. A cam-out lever was attached, as you see at the top of the slide on the right, and then a force was applied to the cam-out lever. The testing was done on four fresh samples and it was found that a torque of 449.5 inch-pounds was required to dislocate this construct from the shell. The standard error on this was 24.7.

Also tested was the one fatigue sample that I showed you in the previous slides. This component had already gone through ten million loading cycles, and it was found that the torque required to dislocate the free fatigue insert was somewhat greater than for that of the fresh samples. At the time it was determined that the reason for the greater torque resistance of the fatigue sample was probably work-hardening of the polyethylene around the locking ring.

The history of this device is that it has been on the market since soon after April of 1989 when substantial equivalence was determined by FDA. And since that time 1224 of them have been sold in the U.S. as of the time of the submission of the PMA, and up to 5/97 1457 have been sold in

the U.S. You will note that a few have been sold in countries outside the U.S., the majority of these being in Japan.

Now, Osteonics distribution of this device is quite unusual for the company. This device is handled in a way quite unlike any of the other implants that the company markets. The distribution usually is on a case by case basis. That is, Osteonics communicates with a surgeon who wishes to implant the device and obtains his agreement that he will present to the patient the limitations of function, seen on the right slide. This is that the range of motion, once a patient has been implanted with this device, is significantly constrained. It is only up to 82 degrees full arc of motion. This implant should not be placed in active or overweight patients, and by overweight Osteonics arbitrarily chose a weight of 180 pounds for the patient. And if dislocation occurs, closed reduction of the hip may then be impossible because of the impossibility of putting the bipolar back through the retaining ring.

All of the surgeons who have used this device have either signed a document on a case by case basis that they will give this information to a patient, or for the 20 or so surgeons who use these devices fairly regularly, where Osteonics allows these surgeons to keep these components on

their shelf, the surgeon certifies that as a group he will give these information to any patient receiving this constrained insert.

Indications for use are given as this: In patients prone to recurrent dislocation, either due to joint instability, anatomic insufficiencies, medical infirmity, or neurologic impairment, this device should be used as an alternative to hip joint fusion.

Indications for use are also stated to be chronically dislocating, total hip replacement patients, again, as an alternative to hip-joint fusion.

Each population for this component is recommended -- where the component is recommended as a salvage strategy, and we understand that this niche population is a tiny fraction of the total hip population in general.

As I said before, one alternative to this treatment is hip-joint fusion. The second alternative is conservative treatment, perhaps a wheelchair, although the conservative treatment may, of course, require surgery to remove the components that are already dislocating in the patient.

Now, in the 1980s when Osteonics had available to put this PMA together, they managed to track little more than 10 percent of the patients who had already received

these constrained inserts, and I would like to present to you two follow-up studies. There are no controls to these studies, of course. This is retrospective data.

The first one was conducted by Dr. Capello, at Indiana University, and Dr. Johnston, in Iowa. The data for these two surgeons is pooled. The indications for use of these two surgeons, not those necessarily recommended by Osteonics, are recurrent dislocation and, in fact, in this data pool the mean is 5.6 previous dislocations per case; medical infirmity, including neurological problems; and for the elderly patient or often elderly patients their inability to follow the standard postoperative protocol associated with total hip replacement. They also looked for intraoperative instability. If, in fact, they cannot achieve a stable hip maybe even in a primary case, then under those circumstances this may be a case where this constrained insert would be used.

The study demographics for Drs. Johnston and Capello are as follows: 101 cases have now been followed up for this PMA. There were the two surgeons, of course, and 97 percent of those cases are patients who were undergoing revision. The mean was 2.5 previous procedures per case for those 97 percent. The mean age is 70 years and now the mean follow up for this group of patients is 54 months.

Clinical results showed that 88 percent of the patients who had received the constrained insert had none or only mild pain; 72 percent of them limped, often due to lack of abductor muscles; and 90 percent of them can now ambulate with and also without support.

Radiographic results show that 95 percent of these patients have acetabular stability. The shells are either bony stable or fiber stable. And on the femoral side, 94 percent of the femoral components are stable.

Adverse events reported in these 101 patients are that there have been 4 dislocations, usually of the bipolar out of the locking ring; 7 patients have had infections and have been revised again; and there have been 2 cases of acetabular loosening, one of which was loosening from acetabular allograft.

That was the first study. Now, in the second study in which this particular surgeon had these indications for use -- abductor insufficiency, recurrent dislocation, multiple revision of these patients, advanced age and, therefore, inability to follow postoperative protocols, and also proximal femoral allograft with lack of abductor muscles.

This study was conducted by Dr. Paul Pellicci at the Hospital for Special Surgery. He now has 21 cases of

these constrained inserts. One surgeon, of course. One hundred percent of these 21 cases were for revisions. The mean age is 69 years. The mean follow up is now 27.5 months.

Dr. Pellicci scored these patients using both the Hospital for Special Surgery scoring system and the Harris Hip Scoring system. His latest evaluation shows, for the Hospital for Special Surgery scoring system, a mean score of 32.2 out of a possible total of 40, and for the Harris system a mean score of 82 out of a possible 100. We have to remember that these are very compromised patients in the first place.

There have been no constrained insert-related failures. He has two clinical failures. One was failure of a structural allograft, acetabular allograft, and one was osteolysis of a femoral allograft, which the surgeon says was not due to the constrained insert.

If we compare these data collected by Osteonics to the available literature on patients with recurring dislocation, we find the following: Back in 1992, Daly and Morey published a number of cases, 95 cases of patients who had recurrent dislocation. They followed them for 7.6 years. They treated them with a number of dislocation preventing procedures and found that at mean follow up they had a depressing redislocation rate of 39 percent.

Kaplan published in 1987, in the Journal of Arthroplasty, follow up of 21 cases where he had tried to strengthen the abductor muscles. At 2.7 years follow up he still had a redislocation rate of 19 percent.

And a study published in the U.K., really the senior author Wroblewski, with 21 patients, redislocation rate of 24 percent, although length of follow up was not clearly given in the article.

If we compare those data in the literature to the data collected by Osteonics, we see Johnston and Capello, with a mean follow up of 54 months with a 4 percent dislocation rate. Pellicci has a zero percent dislocation rate at 27 months. And David Lewellan, from the Mayo Clinic, reported to Osteonics 34 cases with approximately 15 months follow up and no dislocations.

So, clearly, the Osteonics constrained insert is doing significantly better for these patients than other procedures performed and written up in the literature.

I would like to give you two or three anecdotal case histories. This one is from Dr. Douglas Padgett, from the Hospital for Special Surgery. He operated on a 30-year old female with DJD. She was a recurrent dislocator, had 2 unsuccessful total hip replacements and significant diminished quality of life. She ha hyperlaxity of her joints

and the surgeon decided to use the constrained insert. He now reports that one year postop the patient is a typical soccer mom, whatever that means, now participating in raising her young children and being an active member of the community.

Dr. Padgett says that the potential removal of this constrained insert from the market is a tremendous setback in the management of complex primary and revision hip arthroplasty.

Case two, from Dr. Joseph Diamond in the Peachtree Orthopaedic Clinic, Atlanta, the primary total hip replacement with multiple dislocations, 18 months post-index operation, patient has extreme anxiety about the possibility of recurrent dislocations. Revision surgery revealed well a fixed socket, removal of which would in a couple would have required destruction of the bone supporting the implant. He placed a constrained insert and 16 months postop the patient has not dislocated, has no pain and retains good function.

Dr. Diamond says this is an option that we need available in order to give the best care to the patients. By "this option" he means the constrained insert.

Case number three, a 75-year old male with a history of at least two total hip replacements with recurrent instability due to severe abductor insufficiency.

This patient became wheelchair-bound and Dr. Nessler, at St. Cloud Orthopaedic Clinic in Minnesota, performed a revision using a constrained insert. Four years postoperatively, despite the continued abductor insufficiency of this patient, the patient has returned to a reasonable ambulatory life style.

Dr. Nessler says that the patient with instability not amenable to other surgical options would have been severely disabled or even wheelchair-bound without the constrained insert.

And the final case history, this is an 84-year old male, primary total hip replacement back in 1988, experienced multiple dislocations which severely compromised the activities of daily living. He was revised on 3/90 and revealed no functional abductor muscles. He was implanted with a constrained insert because no other reasonable option was found. He returned to full activity eight weeks postop and he now has unrestricted activity, and we must remember that he was 84 when he had his first hip, including the occasional game of tennis.

The slide on the right shows his preop case, pre-the constrained insert case. This is the situation where he was recurrently dislocating. The cup does not appear to be in a very compromising position but, nonetheless, this

patient continued to dislocate because of his weak abductor muscles.

On the left slide we see his postoperative constrained insert. You can see the locking ring which goes around the constrained insert and keeps the bipolar in place clearly outlined against the neck of the hip. And at follow up at 10/93 we see the implant is still fully intact and this patient was still seeing very good function in spite of his compromised musculature.

A few other surgeon testimonials -- David Lewellan who supplied the data in the summary, states the availability of this technique which reliably eliminates recurrent instability represents a major advance.

Dr. Pellicci says that to remove this component from the market would constitute a great public injustice. Patients who have been in the untenable situation of having recurrent dislocations have a reasonable quality of life.

And the final one from Dr. Wayne Paprosky, at Rush Presbyterian Hospital, states although this product is obviously not my first choice, there are instances where it is my only choice. I have to choose between leaving a patient wheelchair-bound or give her the opportunity to walk again without recurring dislocations of her hip.

So in summary, the s urgeons that Osteonics has spoken to are distressed about the potential elimination of this device from the market for this niche population. Without this device the niche population will be left with unacceptable alternatives. And we must remember here that Osteonics very carefully defines to these surgeons the potential risks that the patient sees, including the risk of not being able to do a closed reduction if this device does, indeed, dislocate.

We believe that the potential risks are deemed acceptable when weighed against the potential benefits of the device, and we believe also that the valid scientific evidence which has been presented here supports keeping this device on the market for this very defined, quite small population of patients who recurrently dislocate after total hip replacement. Thank you.

DR. BOYAN: Thank you. Are you through with your presentation?

MR. KOCH: Yes.

DR. BOYAN: Why don't we go right over to the FDA's presentation? Erin Keith is the lead reviewer for the FDA.

FDA Review, Erin Keith

MS. KEITH: Good afternoon, ladies and gentlemen. The PMA product under consideration at this time is the Osteonics Constrained Acetabular Insert. The applicant for this device is the Osteonics Corporation of Allendale, New Jersey, and I would like to thank them for giving an excellent presentation.

The primary review team for this submission consisted of myself, Erin Keith, as the lead reviewer, and Dr. Stephen Nightingale as the clinical reviewer, and T.C. Lu as the statistical reviewer.

Our presentation today will be brief. I will describe to you the proposed indications for use, the device itself and some preclinical studies provided by the applicant. Dr. Nightingale will describe the clinical studies. When Dr. Nightingale has concluded his comments I will present to you questions on which the FDA is seeking the Panel's comments and advice. The questions will look very familiar.

The proposed indications for Osteonics' constrained acetabular insert is for use as a component of the total hip prosthesis in primary or revision of patients at high risk of hip dislocation due to a history of prior dislocation, bone loss, joint laxity or intraoperative instability.

As the name of the device suggests, this is a constrained acetabular insert. The device design is a bipolar head captured within an ultra-high weight molecular polyethylene head. While not necessarily completely accurate, a good way to visualize this device is to think of it as two concentric hemispheres. The inner hemisphere or the bipolar head is constructed from ultra-high weight molecular polyethylene, backed by a cobalt chromium alloy shell. This component also has a pre-assembled ultra-high molecular weight polyethylene retaining ring for the femoral component.

The outer hemisphere is also constructed from polyethylene. It has a 10 degree overhand on one side. The mouth of this component is smaller than its inner hemisphere. The mouth of the component is also encircled by a titanium alloy retaining ring. Below the 10 degree overhang the outer perimeter of this component is encircled by a cobalt chromium alloy wire which incorporates with integral barbs with any appropriately sized Osteonics metal-backed shell.

The entire bipolar outer polyethylene liner assembly is pre-assembled by the applicant at the factory. The entire assembly is captured within any standard metal-

backed shell or any standard femoral head component can be intraoperatively snapped into the bipolar bearing insert.

The device would be available in thr ee inner diameters and five outer diameters. The size range fits any of the Osteonics marginal metal-backed shells with a 52 mm or larger diameter and any appropriately sized Osteonics femoral head component.

The applicant's description of the preclinical data was complete and, therefore, I will not go into great detail concerning its testing. In general, the preclinical data provided by the applicant described the device. However, in brief summary, the applicant has provided the results of sterility, shelf life, biocompatibility, toxicological and mechanical testing of the device.

The sterility parameters provided by the applicant were validated per Amy method for irradiation sterilization. The applicant has also provided validated shelf-life testing out to seven years, indicating the packaging is capable of maintaining sterility for that period of time.

The materials used in the construction of this device are typical of materials found in most semi-constrained total hip devices. Even though there were no new materials used in this device, the applicant did provide results of some biocompatibility and toxicological testing

of the materials. There were no surprises with these results.

Osteonics has already described in detail the mechanical testing they provided. Therefore, I will not repeat their efforts by going into great depth about the methods or the results. Briefly, the testing provided by the applicant attempted to examine the potential mechanisms of failure for the device, those being failure of the titanium retention ring; separation of the femoral head from the bipolar component of the assembly; separation of the bipolar component from the outer polyethylene liner; and separation of the entire device from the metal-backed acetabular shell. In addition to this, the applicant also examined the loads necessary to properly seat the entire device within any metal-backed shell.

Dr. Stephen Nightingale will now present the clinical data.

Presentation by Dr. Stephen Nightingale

DR. NIGHTINGALE: Th e clinical data that the sponsor submitted to us relative directly to this device consisted, as you have heard before, of the two retrospective reviews of the device in clinical practices, review of Medical Device Reports and letters from eleven physicians who used the devices in their practice. The

sponsor has already summarized those eleven letters from the physicians, which they call testimonials, and we will simply refer to as letters, which are also summarized in the review I believe you all got a copy of, and I think you can make your own judgment of our summaries. They did overlap considerably and I have no objection to any of the factual extraction of the material that the sponsor presented.

Regarding the two retrospective reviews, the conclusion is similar. I would be repeating what they have said. In the first study of the practices of Drs. Johnston and Capello, they had collected a total of 98 patients and, again, I will point out this was 101 procedures in 98 patients so that you will see sometimes retracting data per procedure and sometimes data per patient. It is pretty close but it is not exact. The mean age, I got 72 and they got 70. This is not a point on which FDA wishes to take a major stand. The percentage of females -- the mean weight in pounds, however, I will point out was a mean of 161. The range went from 100 lbs. to 286 lbs. As they noted, most of the patients in the Johnston and Capello practices had previous procedures, 97 out of 101 procedures were done in patients who had had a previous procedure. The average number of procedures in those 97 patients was 2.5, with a range of 1.9.

I will go to the next slide to show you the Pellicci data. I couldn't fit them all on one slide but the point of the next slide is that the patients in the second series seemed to be comparable to those in the first. In this particular case from Dr. Pellicci, there were 21 procedures in 20 patients. The mean age, 69; percentage females, 76. And, again, the mean weight in pounds, 154, nevertheless, ranged from 114 to 198. In this particular study we did not have numbers of previous procedures or the average numbers that they had.

In the next slide, the review of the Johnston and Capello combined series showed that roughly half of the patients in the series had osteoarthritis as their underlying disease. A substantial number had trauma. And you can see the remaining list of diagnoses there. Where it says miscellaneous for the 20, I can go over this: 3 of those had tuberculosis; 2 of them had intraoperative instability; two had polio. There were 12 lupus cases in this practice; and 1 was late herpes disease. The underlying diseases in the Pellicci study were not provided in the retrospective review.

Here you can see them side by side in comparison. The patients are not identical by any means, but we consider them to be comparable, prior dislocation being present in

the majority of the cases of Johnston and Capello, and in 7/21 patients in the Pellicci studies.

The matter of interest, of course, is the pati ent outcomes, which I have summarized here for the two. The follow up in the Johnston and Capello was substantially longer than in the Pellicci series. The outcome variable of greatest interest in the sponsor's presentation was subsequent redislocation. There were only 4/98 patients in the Johnston and Capello series; redislocated in the Pellicci, 9/20 patients.

To break this down a little better, however, we, as the sponsor also did, looked at subsequent reoperations, 16 in the 98 patients in Johnston and Capello and 2 out of 20 in the Pellicci series.

To give you a rough idea -- well, I should give you a precise idea of why the patients had reoperations, 4, as you see above, were for dislocation. Seven of the patients in the Johnston and Capello had reoperations because of infection; 2 because of loose acetabular cup; 1 for a loose femoral stem; 1 for excision of a trochanteric wire; and 1 because of a fracture below the femoral stem -- 2 femoral, 2 acetabular.

In the Pellicci series, the two required reoperations did so because of collapse of the acetabulum in

one case and because of osteolytic reabsorption in the femur in the other case. Those are the primary outcomes of the study.

The Medical Device Reports -- I described this morning a procedure for search in this general area. When we searched for this morning we used the same algorithm to search as we used for the current application. Our search identified the same number of Medical Device Reports for the subject device that the sponsor did, and all three of those described recurrent dislocation. There is no other safety data that we uncovered in this search, nor anything else that would impact on our determination of safety or efficacy of the device.

MS. KEITH: I will now present the questions for which the FDA is seeking the Panel's comments and advice, the first being, is the following proposed indication for use supported by the PMA information for the subject device? I won't read the indication; you have already heard it.

What are the ap propriate contraindications, warnings and precautions for the device?

Should the indications be limited in any way?

Should there be limitations on the usage of the device for certain patient populations?

Based on the data derived from the clinical studies or other sources of adequate scientific evidence for the Osteonics Constrained Acetabular Insert, are specific clinical evaluations or tests needed for the selection of patients for the device?

Because of the constrained design of this device, should there be any special instructions for the short-term or long-term patient management, including activity restrictions?

Should any additional or special instructions be added to the surgical technique for total hip arthroplasty when using the Osteonics Constrained Acetabular Insert?

Finally, is a separate patient information sheet necessary for the Osteonics Constrained Acetabular Insert? If so, what type of information should be contained in the patient information sheet?

And that concludes our presentat ion. Dr. Boyan, back to you.

DR. BOYAN: Thank you very much. Since we are moving along so nicely, why don't we go to our two reviewers from the FDA Panel, and ask Dr. David Nelson to give the clinical review?

Panel Review, Dr. David Nelson

DR. DAVID NELSON: I don't have anything of any profound importance to say on the clinical studies. The applicant noted that they weren't prospective. Certainly, that is okay because this is, by necessity, retrospective. They also apologize for being not controlled and I actually have no problem at all with that. In fact, developing a controlled study sometimes is difficult because it would be unethical to have the control. So, certainly, the indications seemed to be fairly clear and I, as a surgeon, would be uncomfortable doing one of these and having a control population. So I have no objection at all to either it being not prospective or not controlled. I don't think you have to apologize for it.

I think there is adequate data in the studies in general to understand that these are safe and effective, and I don't think I have anything more to say.

DR. BOYAN: Thank you. Dr. Markolf?

Panel Review, Dr. Keith Markolf

DR. MARKOLF: Yes, basically I was interested in the failures in the mechanical testing, particularly interested in the four failures which averaged about four percent in one of the studies. It was of particular interest to me that two of the failures were at the shell-bony acetabular interface. One of those occurred at four months

in which the shell dislodged from the cement mantle. The second, on a different patient, occurred at 53 months and, again, it was dislodged from the bony acetabulum. There was an additional failure in which the plastic component pulled out of the metal backing at 17 months. Then, finally, there was one which we saw where the retaining ring of the pre-assembled device was found to have dissociated, resulting in a dislocation.

In terms of mechanical testing, the capture forces are really quite high. It is a fairly complex unit and I have difficulty trying to understand it just from the drawings. It would certainly be nice to see one in front of you and it would answer a lot of questions. There are a lot of different assemblies here, one of which is pre-assembled, and that basically has a very strong capture moment, averaging around 450 inch-pounds of torque, of lever-out moment.

Also the cam-out of the femoral ball depends upon the size of the head, and basically for the 41 mm head it ranged from around 300 pounds up to the 52 mm outer diameter up to around 460, 490 pounds, again, a very strong capture mechanically. They also did some repeat testing for a different size and it fell right in the range of the other devices, around 331.

So it is a very strong mechanical capture. They have also done extensive testing in terms of the push-out force required to dislodge the plastic insert from the metal shell. I am probably not using your proper terminology. And, again, these are very strong forces of capture. So the device seems to be fairly secure mechanically. Once w get into the questions, you know, we can talk about what it actually means, but the mechanical testing has been adequate and fairly extensive.

DR. BOYAN: Thank you very much. This is a post-prandial moment. So everybody can stretch a bit and then we are going to start the questions. Okay, stretching has happened right now. I am going to open the Panel to the question and answer period. Questions can be addressed to people from Osteonics, to the reviewers from the FDA, to either of our primary reviewers, and we will begin the question and answer period with just, again, the general questions. We will go around the room. We will start this time with Dr. Roger Nelson and go in this direction. And everybody, take this opportunity. You can ask one or more questions and then move on to the next person until we have all had a chance to ask the issues that are of concern to us. Dr. Nelson?

DR. ROGER NELSON: I have no additional questions at this time.

DR. BOYAN: Okay. Let's g o to Dr. Silkaitis next.

DR. SILKAITIS: Likewise, I have no questions at this time.

DR. BOYAN: Dr. Holeman?

DR. HOLEMAN: I have no questions.

DR. BOYAN: Dr. Skinner?

DR. SKINNER: Yes, Dr. Boyan, I would like to ask a couple of questions.

DR. BOYAN: I thought you might.

DR. SKINNER: I am going to leave a couple of questions for Dr. Markolf and then I would like to ask another question if he doesn't ask the question I think he is going to ask. But I wanted to ask a couple of things for my information. First of all, the range of motion of this thing is 82 degrees, and that is not variable depending on the head? And that is dependent on your neck diameter? Is that right?

DR. MANLEY: This is Michael Manley. Yes, it is dependent on the neck diameter. The 26 mm head, according to the data we have here, is 82 degrees. With the 22 mm head that can drop to 70 degrees. so it is dependent upon the diameter of the femoral neck before impingement occurs.

DR. SKINNER: That would be extremely important for the surgeon to understand in placement of the prosthesis in the pelvis since that gets down to just barely an adequate range of motion.

DR. MANLEY: You are correct. These people have a barely adequate life style to start with. And the surgeon is informed in writing of what these ranges of motion are, and signs a document with Osteonics stating that he understands that, and also stating that he will pass these data on to his patient.

DR. SKINNER: You are preaching to the choir. I agree. These people are severely compromised by the dislocation. The bipolar is self-righting?

DR. MANLEY: Yes, it is. It is the standard Osteonics universal head replacement. So dynamic loads cause it to get back into a neutral position.

DR. SKINNER: And regarding the bipolar and the polyethylene, with all these bearings in there, what is the minimum thickness of the polyethylene in the largest heads, smallest cup, and what is the thickness of the cobalt chromium?

MR. CYMBALUK: William Cymbaluk, hip and upper extremity steering team for Osteonics. The minimum thickness

of the polyethylene is 4.2 mm, and I don't know the minimum thickness of the cobalt chromium.

DR. SKINNER: I will pass at this point.

DR. BOYAN: Dr. Greenwald?

DR. GREENWALD: I too would concur with Dr. Markolf that there seems to be -- there doesn't seem to be, there has been an extensive amount of mechanical laboratory testing, which surely substantiates the concept. My questions are really developed around the fact that we have multiple articulating surfaces against polyethylene, and I wonder what the company feels. I mean, we have talked about -- I looked at the Pellicci and Johnston total of redislocations and I wondered whether or not they suspect or have any feelings about the increased potential for debris generation, given the fact that we have multiple surfaces now on articulation. It could be three; it could be four if I have interpreted it correctly.

DR. MANLEY: Of course, we do have multiple interfaces but the motion at any one of these interfaces is less. I mean, you either get full motion at one interface, partial motion at that interface and the difference in motion is taken up elsewhere. So the actual arc that you sweep in this component from interface to interface is obviously going to be different because of the different

radii of the interfaces, but we do not believe that there is any evidence to suggest that the wear of these components is excessive and, certainly, the clinical data shows no evidence that there is excessive wear occurring or an excessive incidence of osteolysis with these components.

DR. GREENWALD: I would certainly suspect from just looking at the potential mechanic kinetics and motion of the surfaces that the sliding distance between any one surface with respect to the others is likely to be less than a single hip articulation. So it is just an interesting perspective that you have multiple surfaces, metal on plastic, articulating.

The second question I have relates to the outer shell. Now, from our own evaluations in the laboratory I note that we have at minimum one, an apical hole, and two, with nine potential holes. I just wondered in what variety is the outer shell offered. Is it offered with just the apical hole? Is it offered with screw holes?

DR. MANLEY: No, there is no -- within the constrained insert component there is no shell supplied.

DR. GREENWALD: No, but it can articulate against any shell --

DR. MANLEY: Right.

DR. GREENWALD: Right, I recognize that. But the point of my question is that increasing the number of holes decreases the potential conformity between the outer liner of the constrained device and the inner surface of the fixed shell that you are putting it into. And I just wondered do you have any idea of the kind of shell surfaces that Pellicci and Johnston put these into? Were they screwed in? Are you following me?

DR. MANLEY: You mean do these multiple hole shells have screws in --

DR. GREENWALD: Right, because it seems to me the larger the number of holes in the acetabular shell, the greater the potential for material damage at that interface. I am just curious to know.

DR. MANLEY: That question was never specifically asked of the surgeons. The earlier data will have no screw holes with one particular type of cup and six or eight with another type of cup.

DR. GREENWALD: Okay. Well, I mean, I know from our own evaluations in the laboratory, Dr. Manley, that we have looked at one with an apical hole. We have looked at a maximum where there were nine holes. And it would seem to me that the one with nine holes would offer less of a surface for potential contact, ergo, greater stresses among the

contact surfaces. And I was just curious to know if that was a concern from the manufacturer that cups that have a maximum number of holes might increase the potential risk of material damage to that outer polyethylene liner.

DR. MANLEY: No, we don't think so because we have done testing on Osteonics acetabular shells and have yet to prove or disprove that increasing the number of screw holes in the shell therefore increases the stresses on the back side of the liner and, therefore, leads to greater damage of the liner. We have yet to find any difference between them.

DR. GREENWALD: Okay, thank you.

DR. BOYAN: Thank you, Dr. Greenwald. Dr. Rudicel?

DR. RUDICEL: One request, you said that you had one of these devices, if you could pass that around I would love it --

DR. MANLEY: Here.

DR. RUDICEL: Great. I think you had one with the femoral head also. And just a minor point, you mentioned that surgeons contact Osteonics ahead of time and you talk to them about the appropriate indications. I am curious, in Johnston's study, for example, 30 patients had the device because of intraoperative instability, meaning that he might not have known he was going to use it ahead of time. Do you talk to them afterwards or what is the situation with that?

MR. KOCH: I don't believe we talk to them afterwards. We inform them of what we stated we did here, and then they use their medical judgment, obviously, as to how to utilize the device. I mean, they must have an indication that this device may be needed in surgery. Dr. Johnston, I will be honest with you, is one that has one of the blanket approvals that Dr. Manley discussed, in which he gets a script, if you will, for these devices to be able to put them on the shelf and then have them available should he need them. But he has certified that in his usage of the device he will inform his patients.

DR. RUDICEL: So in another surgeon's inst ance, for example, who might not be using them very often, they would have to have thought about it ahead of time, called Osteonics and gotten the product.

DR. MANLEY: That is correct. Lt me make that completely clear. There are two types of surgeons that use these, one who is a casual user, if you like, and that person has to call Osteonics on a case by case basis. The second one is a more than casual user, like Capello and Johnston who use them fairly regularly, and then they have a script with Osteonics which allows them to keep them on the shelf. Under those circumstances, of course, they can use them intraoperatively.

DR. RUDICEL: Thank you.

DR. BOYAN: Dr. Rudicel, while you are looking at the sample, shall we go ahead?

DR. RUDICEL: Yes, I have finished.

DR. BOYAN: You have finished? Okay, Dr. Rangaswamy?

DR. RANGASWAMY: I don't have any questions.

DR. BOYAN: Dr. Besser?

DR. BESSER: I have one question. You discussed the possibility of doing a closed reduction. After this joint has dislocated is the acetabular insert still viable as far as being able to relocate the hip? And have you done any studies, either bench-testing where you have dislocated the hip and then relocated it and seen what you have lost in strength?

DR. MANLEY: The point here is exactly the reverse of that. The point here is that it is almost impossible to do a closed reduction because if the failure occurs between the bipolar and the constrained liner then, that had already been pre-assembled in the factory. You cannot do that intraoperatively. If the failure occurs between the plastic liner and the acetabular shell, there is a locking ring in there which, again, you cannot put in during closed reduction. So the warning that is given to patients is if

this implant dislocates it is almost impossible to put it back without going to open surgery.

DR. BESSER: I am curious about your use of the word almost.

DR. MANLEY: Well, I should not say almost. It is completely impossible to put it back without --

DR. BESSER: I f the dislocation were at the femoral head juncture -- you have most junctures than most, but if it were the femoral head coming out of what I will call the acetabular insert --

MR. KOCH: Bipolar.

DR. BESSER: Right, the bipolar insert, then could that be reduced possibly in a closed surgery, without opening it, and if it were reduced in that manner, what is the loss in strength or integrity of the prosthesis?

DR. MANLEY: There is a tiny chance that it could be reduced, but the problem is if the head comes out of the bipolar, the only way it can come out is by the damaged locking ring inside the bipolar. So under those circumstances, if that came out, there is a 99.99 percent chance that the surgeon will go back into the hip because there is something damaged with the component.

DR. BESSER: Okay. And in any one of these open reductions the acetabular insert would be replaced?

DR. MANLEY: Yes, it would.

DR. BESSER: Okay, thank you.

DR. BOYAN: Let me get the Panel back on task here. I have two things, one is a comment that I only wanted in the record, it is not really applicable to the head component but it is applicable to some of the data that you presented as preclinical data. Since this is a unique situation, or not unique but it should not be very common or ongoing over a long period of time, in the FDA, these calls for former 510(k)s, I am not going to go back and say that the testing, the preclinical testing was inappropriate because a decision was made based on that preclinical testing. But in the future I would like to have the FDA reconsider how they look at tissue compatibility with materials that are going to be primarily in bone; that looking at tissue compatibility in muscle may not be the most appropriate place to look.

In this case you have shown data not only for the titanium component, the cobalt chrome component, but also for both materials coated with ceramic. And in all four materials, while the studies were done certainly within regulations, I would question that muscle is the appropriate tissue to test that in. Muscle is not the appropriate tissue and bone is the appropriate tissue. Bone in contact, not

only cortical bone but bone in contact with marrow would be a more appropriate testing site.

Then I would like to just support Dr. Greenwald's comments on the polyethylene. These devices will go primarily into people with lower levels of mobility but not exclusively, and there is a considerable amount of polyethylene there that has plenty of opportunity to wear away, and even though wear is minimal, with that many articulating surfaces any wear that can accumulate, if it does accumulate has a negative consequence to the patient. And I think in younger people or more active people that might be a more important problem than it would be in a more sedentary individual.

Now I would like to turn to Dr. Nelson.

DR. DAVID NELSON: Actually, I would like to just ask one simple question both of Dr. Greenwald and of Dr. Markolf. The cyclic test of the device, when they tested came out was much higher, and they thought it might be to the work-hardening of the polyethylene. Is that a reasonable explanation?

And following up on your questions earlier this morning, Seth, of testing with cyclic testing, do you think it is useful to recommend that that be looked at further?

DR. GREENWALD: Well, I certainly think that in this instance they certainly did test in a cyclic manner. And I think that I was satisfied with the cyclic nature of the load application. I think that work-hardening argument is not an unreasonable one. I think that, yes, it can -- polyethylene I think can be work-hardened, particularly as you simply deform it within its elastic range, and beyond its elastic range you can also work-harden it. So I think that those comments are appropriate. I don't think they are inadequate.

DR. DAVID NELSON: It is just that that one test was outside the standard deviation of their other ones, and, you know, it was several times that. So is that a reasonable explanation or is there a need to really do some more tests?

DR. GREENWALD: Well, when I read the data I couldn't really think of another rationalization as to just why there was such a difference in the standard deviations that you referenced. But I would like to ask perhaps the company. Are there any other thoughts about that, Dr. Manley, as to other than work-hardening that might be an explanation for the increased apparent retention?

DR. MANLEY: Well, we certainly racked our brains at the time that testing was done. I mean the testing was done some years ago now, and that was the only rational

explanation we could come to at the time. No, we are stumped. It was the only reasonable explanation.

DR. SKINNER: Could it be, Dr. Manley, that you did it at 30 Hz and you heated the plastic?

DR. MANLEY: That is a possibility I suppose, although in those days we did not measure the temperature of the components.

DR. GREENWALD: Thirty Hertz is pretty quick, Mike.

DR. MANLEY: Twenty Hertz.

DR. GREENWALD: Even that is pretty fast. I mean, that is hot time, I would think, unless you cooled it in some manner.

DR. MANLEY: Right --

DR. BOYAN: Gentlemen, gentlemen, comments? Some of those comments were by Dr. Greenwald and some of the comments have been by Dr. Skinner and some of the comments have been by Dr. Manley.

DR. GREENWALD: Yes. You tested at 20 Hz, and I said that was hot time. I know that when we test polyethylene in the laboratory we are certainly down to around 2-5 Hz and often times cool. And I guess one question is was any attempt at cooling made that you can remember

from these tests, and I recognize they were done a while ago?

DR. MANLEY: The information that we have here is that there was some attempt made to measure the temperature of that test. Is that correct?

MR. CYMBALUK: William Cymbaluk. Yes, some attempt was made to measure that test. I don't remember the value offhand. It was no more than approximately 90 degrees Fahrenheit, the heating, during that testing period.

DR. GREENWALD: What does that mean i n centigrade?

DR. BOYAN: Are we in a scientific exchange that we can understand? What is the point of this discussion?

DR. GREENWALD: Well, the point of this discussion is was the temperature raised sufficiently enough to cause damage to the polyethylene and alteration in its structure? And at 90 degrees Fahrenheit, as my colleague here is informed me, is about 35 degrees centigrade, and the body temperature is 37 degrees centigrade so it is unlikely that the temperature played a role, although I am surprised that the temperature was that low at 20 Hz, but if that is what your thermocouples, or whatever device you used, indicated, I will accept that.

DR. BOYAN: And is the answer to this question important or germane to our discussion of the product?

DR. GREENWALD: Well, it could be germane to the apparent increase in the capture ability of the mechanism. But if that temperature is as they said it is, that is well within the body temperature ranges.

DR. BOYAN: Okay. Dr. Manley, is there anything you want to say in response?

DR. MANLEY: No.

DR. BOYAN: Okay. Dr. David Nelson, are you complete with your questioning?

DR. DAVID NELSON: Yes. I just wanted to ask Dr. Markolf if he wanted to answer that as well.

DR. MARKOLF: I am always worried about an N = 1.

(Laughter)

DR. GREENWALD: Yes, you have a good point there.

DR. DAVID NELSON: Not only N = 1 but it gives you data you didn't expect. You expect a lower number and it is higher. That scares you a little bit.

DR. GREENWALD: That is a good point actually.

DR. BOYAN: Dr. Markolf?

DR. MARKOLF: You seem to have more of a close control than most companies on who gets these and under what circumstances. So I would also assume that you have control on getting them back, you know, when they fail. Of these four devices that we have had, were you able to examine them

to see, for example, why the titanium ring, you know, came off? Was it a tolerance problem? Have you looked at the components that were reported here?

DR. MANLEY: Let me just answer a bit about the titanium ring coming off. I think I confused the Panel with the slides I showed of Dr. Capello's case. The case I showed was an intact constrained insert. The titanium ring appears to float in space but it is still attached to the polyethylene. So those slides were a success, not a failure. As far as we know, we have not had any with the titanium ring coming off, have we? Okay, I misspoke. There are two cases that the clinical people know of where the titanium ring came off. That was not one of them that I showed. That was a success.

DR. MARKOLF: Were those components returned to the factory for analysis? Because this was a pre-assembly, right?

MR. CYMBALUK: William Cymbaluk. It was a pre-assembled device. We did not receive any of those components back for analysis.

DR. MARKOLF: Did you try to get them back? I mean, since you have control over who gets them and under what circumstances, you know, in the future can you ask?

MR. KOCH: This is Bob Koch. For complaints which come in we certainly have an obligation to investigate those, and we make attempts there. In this instance, this information was retrieved, as you are well aware, from the retrospective basis and the components had apparently been discarded without the ability to review those.

DR. MARKOLF: How is that ring held in place? Is there a little snap, you know, like we saw -- well, we can't talk about what we saw this morning, but how is that held in place?

MR. CYMBALUK: That ring is held by a mechanical groove in the polyethylene and it is assembled by cooling the polyethylene, and then pressing the ring over --

DR. MARKOLF: Is there a little ledge

MR. CYMBALUK: Right.

DR. MARKOLF: Again, this is more of a comment, similar to what we talked about this morning, but I would urge that as a design consideration that maybe some cadaveric testing be done to see, you know, what boundaries you have, and I will tell you why. Because this morning for the device, and I can talk about this because it is public record, it was around 150 inch-pounds of lever-out moment. For your device the numbers are considerably higher. I think the lowest one was around 300 and it went up to close to

600. So there is certainly a more extensive capture or a stronger capture of your femoral ball and the device.

I also noted that in two cases you had a possible -- well, you did have a dissociation of the device from the bony acetabulum. So it actually did pull out. So I am trying to hone in, you know, on this safety fuse, if you will, and the pop-out moment, and I am just wondering, you know, what your thoughts are about that and have you given consideration to maybe loosening the tolerances? You may be a little too high in your capture values.

MR. CYMBALUK: William Cymbaluk. The bet we can do is to test a well-cemented acetabulum in the laboratory, and the 450 pounds is still below the value of a well-cemented prosthesis. It is impossible for us to test --

DR. MARKOLF: And you tested those in cadaveric --

MR. CYMBALUK: No, we tested those in simulated foam pelvises.

DR. MARKOLF: Again, it is just a recommendation. I think if you can get a bound on that number, it may help you down the road in determining whether your device maybe has too much capture because you certainly don't want to dissociate that bony bed.

DR. MANLEY: Absolutely. Let me just make a comment. One of the problems with this type of device in a

patient who is already highly compromised is you really don't know what the fixation is like between the metal acetabular shell and the underlying pelvic structures. One of the ones that failed was, in fact, failure of an allograft, an acetabular allograft. And to simulate an acetabular allograft, of course, is almost impossible.

DR. MARKOLF: Right.

DR. MANLEY: Some of the components are cemented, some are porous ingrowth. There is a wide variety of things. Some of the patients are suffering from maybe not very stable shells but the surgeon might still try to put in his constrained insert in and leave the shell behind for other reasons.

So I think the best we can do is to compare against an idealized standard, if you will, and the best idealized standard we have is this test that is done in the so-called Daro foam which simulates the structures and the mechanical strength of cancellous bone. And under those circumstances, when you test the lever-out of this constrained insert, if you look at the failure cascade, if you will, when you apply a moment into this insert, you firstly tend to dislocate the polyethylene liner within the shell; secondly, the bipolar of the polyethylene liner; and the third -- and the strongest interface in this ideal

circumstance is the cemented interface between the acetabular shell and the underlying simulated bone.

DR. MARKOLF: I agree that testing in foam does have value. In my view, the main value is comparing design A to design B. What I guess I am looking for is just sort of a rough bound of the strength of the human cadaver pelvis and the implantation.

DR. BOYAN: Dr. Skinner, did Dr. Markolf ask the question that you wanted to ask.

DR. SKINNER: he came pretty close, and I think Dr. Manley came pretty close to addressing it. I missed which was the strongest interface. Is it the bone-prosthesis interface? And if so, which one is that?

DR. MANLEY: The simulated bone-prosthesis interface, cemented; the cemented, simulated bone-prosthesis interface was the strongest to lever-out.

DR. SKINNER: And we have no idea what the ingrowth interface prosthesis would be?

DR. MANLEY: We have a ttempted in the past, and I have no data here, to use epoxy compounds to sort of simulate bone ingrowth into these components, but it is not a very reliable way of doing things so the best we can do is to cement a shell and say that our cemented shell is, quote, our gold standard and compare these other things to that.

DR. SKINNER: I guess the reason I am raising this question is I am concerned that -- I am not familiar with the Osteonics cup and I am concerned that the virgin implantation of this shell may not be strong enough. I can understand it being replaced in a revision situation for dislocation, not taking the shell out, putting in a new constrained cup. I can understand that. But I am concerned that when intraoperative instability is discovered and you decide to put in a cup that an ingrowth cup may not be strong enough in the early postoperative period, or even in the late postoperative period, without screw fixation to provide stability to prevent that interface from failing. Was that clear?

DR. MANLEY: You are talking about the situation where intraoperatively a surgeon puts in one of these devices into a press-fit porous ingrowth socket that he has just placed? Is that your concern?

DR. SKINNER: Yes.

DR. MANLEY: Well, the bone ingrowth into the porous socket will not take care of the moment applied by impingement on the edge of the constrained insert. Did I understand that correctly?

DR. SKINNER Yes.

DR. MANLEY: I had a similar concern myself, and that is why we try and put these -- not constraints; it is the wrong word, but this advice out to surgeons about how these devices should be used. But I do take your point that any insert in which impingement is a high probability has a possibility of damaging a biological ingrowth interface before the biological ingrowth is complete. That is quite correct.

DR. SKINNER: I would suggest that this might be helped by screws.

DR. MANLEY: I take your suggestion as reasonable. It certainly would be helped by screws.

DR. BOYAN: Are there a ny other general questions from the Panel? Dr. Skinner?

DR. SKINNER: Back to the wear issue -- I am sorry to hit on this again, but you mentioned 4.2 mm as a minimum polyethylene thickness for a polyethylene piece that is between two metal interfaces, and that is quite thin and I would be concerned, as Dr. Greenwald was alluding to, this being at the outermost polyethylene layer. Is that where the 4.2 mm can be? Because, if that is where it is with screw holes, the contact stresses can be extremely high there.

MR. CYMBALUK: William Cymbaluk. Yes, that is where it is. It is the outer layer of polyethylene. It is a

much broader bearing surface at that point because you are between the bipolar component and the shell. So it is not a point contact like you find in some of the earlier joints where you have a very thin polyethylene between a small diameter head.

DR. BOYAN: Yes, Dr. Greenwald?

DR. GREENWALD: Just driving this a little bit further, in the Johnston study, Capello study, how many f those were cemented and how many of those were uncemented? Can you answer that question?

MS. NAUGHTON: I am Mary Beth Naughton, manager of clinical research at Osteonics. Eighty percent of them were uncemented. I don't know about supplemental screw fixation.

DR. GREENWALD: Yes, I asked that question earlier, did you have any idea of the number of screw holes? I guess I have to express a little bit of a concern about that surface at 4.2 mm in relationship to the number of holes. And it is something that I guess probably you are just going to have to wait and see as time progresses as to whether or not -- I mean, you gain the advantage of better bone fixation to the bony bed with the adjunctive use of screws, but you also diminish the potential contact surface between the outer surface of the polyethylene liner and the inner surface of the acetabular shell.

I noticed as I looked through this, and I just kind of noticed this, are some of these components molded, Mike?

DR. MANLEY: As far as I know, they are all machined. They are all machined, yes.

DR. GREENWALD: They are all machined?

DR. MANLEY: Yes.

DR. GREENWALD: Thank you.

DR. BOYAN: Okay, do we have any other questions or comments? Yes, Dr. Besser?

DR. BESSER: The smallest polyethylene ring on the inside of the acetabular is cut. Is that just for the demonstration?

DR. MANLEY: The ring in the bipolar is made that way so that you can expand the ring to get the head through, and then the head will not pull out through the ring. The ring jams into the mouth of the bipolar insert. If that ring was a solid piece you would have to stretch the ring to get the head in. So the ring just pushes apart to get the head past it, and that design was first produced in 1979 or 1980.

DR. BOYAN: Do we have any more questions or comments? Dr. Besser?

DR. BESSER: Mark Besser. The smallest polyethylene ring on the inside of the acetabular insert is

cut. Is that just for the demonstration one or for the actual one?

DR. MANLEY: Michael Manley. The ring in the bipolar is made that way so you can expand the ring to get the head through. Then the head will not pull out through the ring. The ring jams into the mouth of the bipolar insert. If that ring was a solid piece, you'd have to stretch the ring to get the head in. So the ring just pushes apart to get the head past it, and that design was first produced in 1979 or 1980 and it's been sold all over the world ever since. It's a proven locking device for this particular insert.

DR. BESSER: I wasn't concerne d with its ability to lock in but as just two more edges for potential wear between the surfaces. I wasn't sure whether that's the way it was made or whether that was justÊ--

DR. MANLEY: Michael Manley. That is the way it's made, yes.

DR. BOYAN: Okay. I think that the best thing for us to do is take a 10-minute break. Do you have further questions?

(No response.)

DR. BOYAN: I asked at the very beginning. What we'll do is take a 10-minute break, come back and when we come back, Ms. Nashman will explain to us the voting.

PANEL MEMBERS: Questions.

DR. BOYAN: I forget the FDA questions every time. We do have to do the FDA questions. Do you want to do them now? I really thinkÊ-- I'm going to argue with you on this one, Seth. This group needs a break. We're going to do the FDA questions when we come back.

(Recess.)

DR. BOYAN: The panel is back. Let's start with the questions for the FDA. This is to keep everybody awake. I'll decide who's going to be first. I'll make an assessment as to the first speaker and then we'll go either to the left or the right, so you don't know when you're coming up.

Panel questions. The first question we've been asked to address is the following proposed indication for useÊ-- is our slide person here for putting the questions up on the projector?

The first question: Is the following proposed indication for use supported by the PMA information for the subject device? The Osteonics constrained acetabular insert is indicated for use as a component of a total hip

prosthesis in primary or revision patients at high risk of hip dislocation due to a history of prior dislocation, bone loss, joint laxity or intraoperative instability.

If we don't feel that this statement is supported by the data that they have presented, then FDA has asked us to recommend what we would feel would make an appropriate statement.

And to begin this discussion, let's start with Dr. Rudicel and then go to Rangaswamy. So that's the direction we'll go.

DR. RUDICEL: I think that's an a ppropriate indication, as worded.

DR. BOYAN: Dr. Rangaswamy?

DR. RANGASWAMY: I agree.

DR. BOYAN: Dr. Besser?

DR. BESSER: I agree.

DR. BOYAN: Dr. David Nelson?

DR. DAVID NELSON: I have no objection.

DR. BOYAN: Dr. Markolf?

DR. MARKOLF: I agree.

DR. BOYAN: Roger Nelson?

DR. ROGER NELSON: I agree.

DR. BOYAN: Dr. Silkaitis?

DR. SILKAITIS: No objection.

DR. BOYAN: And Dr. Holeman?

DR. HOLEMAN: I agree.

DR. BOYAN: And Dr. Skinner?

DR. SKINNER: Actually, I see no reason why it shouldn't be the same as the one this morning. I would change it to deficiency of surrounding musculature, bone loss, neuromuscular disorders and/or previous surgery, as I think we did this morning.

DR. BOYAN: Yes. Dr. Greenwald?

DR. GREENWALD: I would concur with that. Seth Greenwald. I would concur with Dr. Skinner's comment.

DR. BOYAN: Is that a general feeling amongst the panel?

PANEL MEMBERS: Yes.

DR. BOYAN: Okay. Then let's move on to the next question. What are the appropriate contraindications, warnings and precautions for the device? Should the indications be limited in any way? Should there be limitations on the usage of the device for certain patient populations?

For this let's begin with Dr. Nelson and we'll go towards Keith Markolf second. Dr. David Nelson.

DR. DAVID NELSON: I have no objection.

DR. BOYAN: Wait. No objection? You have to identify are there any contraindications, warnings or precautions for the device?

DR. DAVID NELSON: Those are written out. It's appropriate. I have no objection to the labeling.

DR. BOYAN: Okay. Dr. Markolf.

DR. MARKOLF: I agree.

DR. BOYAN: Dr. Roger Nelson.

DR. ROGER NELSON: I agree.

DR. BOYAN: Dr. Silkaitis.

DR. SILKAITIS: I agree.

DR. BOYAN: Dr. Holeman.

DR. HOLEMAN: I agree.

DR. BOYAN: Dr. Skinner.

DR. SKINNER: Did we make any changes this morning?

DR. BOYAN: I think we did.

MS. NASHMAN: I'm sorry; you can't discuss that. This needs to stand on its own.

DR. SKINNER: I see. Well, I have no changes. I don't think that weight limits should necessarily be a contraindication.

DR. BOYAN: Dr. Greenwald.

DR. GREENWALD: I would concur with what Dr. Skinner has said.

DR. BOYAN: So you eliminate the weight limit as a contraindication?

DR. GREENWALD: Although I would ask the company, do they have any major objection to doing something like that? After all, it's your number.

DR. MANLEY: Michael Manley. We have no objections to what Dr. Skinner and Dr. Greenwald are saying.

DR. BOYAN: Dr. Rudicel.

DR. RUDICEL: I agree with the contraindications as they're written.

DR. BOYAN: Dr. Rangaswamy.

DR. RANGASWAMY: I agree with what's been said so far.

DR. BOYAN: And Dr. Besser.

DR. BESSER: I agree with what's been said.

DR. BOYAN: And I would just like to add the comment that again, that there be some sort of verbiage to account for the more active patient that may present; not that it be a limitation, that it not be used, but that there be some kind of indication that there may be a slightly different prognosis to be expected with a more active patient.

All right, any other comments on this set of questions?

(No response.)

DR. BOYAN: All right. Going on to the next question, based on the data derived from the clinical studies or other sources of adequate scientific evidence for the Osteonics constrained acetabular insert, are specific clinical evaluations or tests needed for the selection of patients for the device?

We'll begin with Dr. Rangaswamy and go backwards to Dr. Rudicel.

DR. RANGASWAMY: I believe they're already spelled out in the indications.

DR. BOYAN: Dr. Rudicel.

DR. RUDICEL: I would agree there's no other special tests that are indicated.

DR. BOYAN: Greenwald.

DR. GREENWALD: I concur.

DR. BOYAN: Skinner.

DR. SKINNER: Concur.

DR. BOYAN: Dr. Holeman.

DR. HOLEMAN: I concur.

DR. BOYAN: Dr. Silkaitis.

DR. SILKAITIS: I concur.

DR. BOYAN: Dr. Nelson.

DR. ROGER NELSON: I concur.

DR. BOYAN: Dr. Markolf.

DR. MARKOLF: I concur.

DR. BOYAN: And Dr. Nelson, David.

DR. DAVID NELSON: I concur.

DR. BOYAN: Okay. Dr. Besser.

DR. BESSER: I concur.

DR. BOYAN: Next set of questions. Because of the constrained design of this device, should there be any special instructions for the short- and long-term patient management, including activity restrictions?

And secondly, should any additional or special instructions be added to the surgical technique for total hip arthroplasty when using the Osteonics constrained acetabular insert? And we'll begin with Dr. Roger Nelson and move to Dr. Silkaitis.

DR. ROGER NELSON: No other additional constraints.

DR. BOYAN: Dr. Silkaitis.

DR. SILKAITIS: I concur.

DR. BOYAN: Dr. Holeman.

DR. HOLEMAN: I concur.

DR. BOYAN: Dr. Skinner.

DR. SKINNER: Referring back to the comments I made before regarding the attachment of the acetabular shell to the bone, I think that in the fresh implantation of an acetabular shell, it would be cogent to recommend screw fixation of the acetabulum shell.

DR. BOYAN: Dr. Greenwald.

DR. GREENWAL D: For all the potential down sides that can occur with multiple screw holds, in terms of increased contact stresses, I think I would have to agree with Dr. Skinner in this instance.

DR. BOYAN: Dr. Rudicel.

DR. RUDICEL: Just a point of information. You're referring to a noncemented shell?

DR. SKINNER: Yes.

DR. RUDICEL: I would agree with Dr. Skinner.

DR. BOYAN: On the noncemented shell?

DR. RUDICEL: Yes.

DR. BOYAN: So, Dr. Skinner, would you put that addendum in there, that it be a noncemented shell fixation?

DR. SKINNER: Skinner. Yes.

DR. BOYAN: Dr. Rangaswamy.

DR. RANGASWAMY: I agree with what's been said so far.

DR. BOYAN: Dr. Besser.

DR. BESSER: I would also add the caveat that there was something on the slides about if dislocation occurs, closed reduction may not be possible. I don't remember seeing that anywhere in the material presented or submitted before today and I'd like it made clear that closed reduction is not possible. I guess that goes on the physician recommendation.

DR. BOYAN: Yes. Dr. David Nelson.

DR. DAVID NELSON: I agree with Dr. Skinner, although I'm not sure it was stated properly, so I think we should just state it for the record. I think there's a relative contraindication for fresh implantation of this in the ingrowth mode, due to lack of any substantiating data that say it's safe.

Am I correctly paraphrasing you, Dr. Skinner?

DR. SKINNER: Harry Skinner. I think you went the other way, David. I think that what I suggested was that if you use an ingrowth cup, you should use screws and you're saying that you shouldn't useÊ--

DR. DAVID NELSON: No, I'm saying that there would be a relative contraindication for the fresh implantation of the ingrowth unless you're using the screws. You've got to have something that's more than just ingrowth.

DR. DAVID NELSON: Yes, I agree with that.

DR. BOYAN: Okay. And Dr. Markolf.

DR. MARKOLF: I agree.

DR. BOYAN: Any further discussion on this particular set of questions?

(No response.)

DR. BOYAN: W e have one more. Is a separate patient information sheet necessary for the Osteonics constrained acetabular insert? If so, what types of information should be contained in a patient information sheet? And we have not started anything with Dr. Besser.

Dr. Skinner, do you haveÊ--

DR. SKINNER: Could I interrupt?

DR. BOYAN: Sure.

DR. SKINNER: I think that, as we have discussed in the past, it would be cogent to put the information for the surgeon in the surgical technique book so that the surgeon would have the package insert there, rather than have it in the package that he's scrubbed and can't read and it's in little fine print and so forth.

DR. BOYAN: That's a good addendum and I think it's important that we state that. That's in reference to the previous set of questions.

Now, in reference to the current set of questions, which is the patient information sheet, without entering

into the discussion of whether or not having complete disclosure to a patient is good or bad, because we are referring that to staff to work out, with respect to this particular product, is there specific information that should be on the patient information sheet that we need to tell the FDA our opinion on? Dr. Besser, why don't you begin that one?

DR. BESSER: I think that because of the fairly low range of motion, especially with some of the head sizes for the femoral component, I think that some indication for limited range of motion should be given to the patient.

DR. BOYAN: Some indication that they should expect a limited range?

DR. BESSER: That they should expect a limited range of motion and what that range of motion would be.

DR. BOYAN: Okay. Dr. David Nelson.

DR. DAVID NELSON: No.

DR. BOYAN: So let it reflect that Dr. David Nelson thinks there should be no specific information. Okay.

Dr. Keith Markolf.

DR. MARKOLF: I would also say no and I would ask, you know, how can you tell the patient what the range of

motion is going to be, based upon the 82 degrees or whatever it is that tested in the lab? What do you tell the patient?

DR. BESSER: Mark Besser. I'm assuming that would be their maximum range of motion. They would not do any better than that and it could result in significantly less than that.

DR. MARKOLF: Most likely significantly less than that.

DR. BESSER: That's the information that I thinkÊ-- for many patients, if this is being used in an older patient with severely compromised range of motion, it might not be an issue. But if this is being used for other reasons in a younger patient, where range of motion might be an issue, where normally or with a different procedure, they might end up with greater range of motion, allowing them a different quality of life, that might be an issue.

DR. BOYAN: Dr. Manley?

DR. MANLEY: Michael Manley. I just want to maybe re-explain something that probably didn't get over very well this morning, or earlier.

Each surgeon that uses these components certifies that he tells his patient that receives the component that they will, if they do have the component implanted, suffer a reduced range of motion. And whether the patient is young

or old, these patients are all compromised individuals in the first place who are suffering usually multiple dislocations or the probability of dislocation, mainly the first one. They're suffering multiple dislocations.

So they're already very compromised and they're told they have two choices: to have a procedure in which dislocation may still be an issue or this component, where dislocation will be less of an issue but limited range of motion will result.

So that is happening now and the company has made its best efforts to make sure those patients are informed of that before they receive the implant. We can't guarantee the surgeons pass that information on but they certify that they will pass it on before they're supplied the product.

DR. BOYAN: Thank you, Dr. Manley.

I think the issue from the panel's point of view is that we're recommending to FDA that the patient also have access to that information directly, independently of the surgeon, and that that be included as a patient information item.

Dr. Nelson?

DR. ROGER NELSON: Without getting off onto the whole issue again of how much information you give the patient, if the FDA would take under advisement some form of

relationship of this loss of range of motion to perhaps some functional activities that would occur; you know, something that the patient could relate to, because they may not relate to 82 degrees or may not relate to 60 degrees, but they may relate to the fact that they may have difficulty getting in and out of a car or they may have difficulty sitting on a regular size commode, a regular height commode, things like that.

So that's just under advisement and I don't want to get into the issue of that, but I do think, in this device, some consideration be made of that.

DR. BOYAN: Dr. Silkaitis.

DR. SILKAITIS: Yes. The company has made efforts to have the patient informed through the physician. If this device has uniqueness to it, then that should be communicated.

DR. BOYAN: Thank you. Dr. Holeman.

DR. HOLEMAN: I concur that the patient should have an information sheet provided that would be inclusive of the information that Dr. Nelson has just mentioned.

DR. BOYAN: Dr. Greenwald, would you like to make a further comment?

DR. GREENWALD: Not on that question but I do have a further comment I'd like to make.

DR. BOYAN: You do have another comment related to something else?

DR. GREENWALD: Yes.

DR. BOYAN: Okay. Are there any ot her comments specific to this question?

Yes, Dr. Skinner and then Dr. Rangaswamy.

DR. SKINNER: I think that this falls into the area of informed consent and I think it's the territory of the physician. I don't think that we should be getting into this.

I think that a patient information sheet, whether it's stated to be a patient information sheet or what, will quickly, in the eyes of an attorney, become part of the informed consent process and I don't think that's where I, as a surgeon, think that the FDA ought to be going.

DR. BOYAN: Dr. Rangaswamy.

DR. RANGASWAMY: I have to agree that the issue here is what is the information that the company is supposed to provide with this product for the patient? I'm not sure that giving technical information is that useful and we're constantly crossing over into the field, I guess, of informed consent and what the doctor is going to explain to the patient.

These are compromised patients who have already probably had discussions, numerous discussions about this, so I don't think we should get mixed up about that. That bothers me about any product, whether it's this one or anything else. I don't think the patient information sheet, with details about the product, really is that useful to a patient.

DR. BOYAN: Any other comments on this subject?

(No response.)

DR. BOYAN: All right. Hearing no further comments on this subject, Dr. Greenwald, do you want to bring up your comment?

DR. GREENWALD: Yes. I wonder, Dr. Manley, if you could address this. A couple of things have just entered into my head here as we've talked further.

In your instructions of use, the constrained acetabular insert as manufactured by Osteonics, is there verbiage or warnings that it should only be used with a comparable Osteonics product, femoral stem?

DR. MANLEY: Yes, and that's crucial with this component. One of the crucial factors, for example, is the shape of the femoral headÊ-- bearing. There have been instances in the past where some bipolars have been forced to dislocate when they've been used with a femoral head of

another manufacturer, and the design of the bipolar and the design of the other manufacturer's femoral head have not been compatible.

So the labeling here specifically states with Osteonics products.

DR. GREENWALD: Okay. Just let me go on for a moment here. The constrained acetabular insert again is then implanted, snapped onto either an existing Osteonics stem, which is going to remain intact, or a new one at the time of insertion, for a dislocation, and this component then is snapped on.

Is there anything in the instructions that say anything to the fact that this component should not be snapped off again, once it's snapped on? Because I am concerned about this inner ring. I've played with it myself here for a little while and I'm convinced that periodic snapping on and off of this insert will, in fact, offer potential damage to the bearing insert, the circumferential polyethylene retaining ring.

I thought you made a comment on that when I asked that before, but is there any instruction? Does the corporation feel that that indeed should be replaced upon multiple reattachment of the acetabular insert onto a femoral head?

Do you follow what I'm saying?

DR. MANLEY: Michael Manley. Yes. I just need to ask somebody here a question about what Osteonics labeling currently says. Give me 10 seconds.

DR. GREENWALD: Sure.

(Pause.)

DR. MANLEY: Michael Manley. There is nothing in the labeling to state that these bipolar heads should not be removed and reinserted. And, in fact, they have been used, I think since 1979, certainly 1980, not as part of the constrained insert but worldwide as a bipolar replacement for hemiarthroplasty.

The usual customary way of using them is to put them on and leave them there.

DR. GREENWALD: And leave them on.

DR. MANLEY: Right.

DR. GREENWALD: But let's just facilitate a hypothetical situation in the operating room where indeed, for some reason, this bipolar is removed. I've done it a few times here and I can tell you that the opening of the ring, the split ring here, is increased.

DR. MANLEY: Michael Manley. Maybe you're overly rough with it.

(Laughter.)

DR. GREENWALD: Remember now; I am an engineer and not a surgeon.

DR. MANLEY: Michael Manley. In all seriousness, though, you only need to open that ring far enough to remove the head. When you actually remove that component, you are actually pulling on the component and inserting the key.

As soon as the ring opens enough to free the head, the head will come off or come out of the bipolar. Doing so keeps the polyethylene within its elastic limits. So the definition states it'll go back to where it came from. I have never heard of anybody yet taking it to its plastic limit toÊ--

DR. GREENWALD: Well, it just seems to me that it's a logical associated potential for a dislocation. I wonder, in your clinical historyÊ-- bipolars, et al.Ê-- have you experienced any degree of disassociation of this constrained insert in a bipolar situation?

DR. MANLEY: Ten seconds. I have to ask this question.

(Pause.)

DR. MANLEY: Michael Manley. My colleague here says we know of no dislocations of bipolars when the bipolar is in good condition; that is, when significant wear has not

occurred on the interior bearing or some traumatic event has not occurred to the patient.

The other point he makes is that the locking ring that you see on that bipolar, when the head is implanted inside it, the taper on the head tends to push the ring closed?

DR. GREENWALD: Closer.

DR. MANLEY: Right. It has not been a complication. It's not been seen in the many clinical studies on bipolars done in both Japan and the U.S. And it certainly has not been a complication on these constrained inserts that we've looked at.

DR. GREENWALD: Thank you.

DR. BOYAN: Ms. Keith, did you want to add something to that?

MS. KEITH: No, I'm just taking notes.

DR. BOYAN: Okay. Then does Dr. Manley's answer to your question, Dr. Greenwald, encourage you to want to make any other statements with respect to any other questions FDA asked us?

DR. GREENWALD: No.

DR. BOYAN: Dr. Witten, did we address the issues that you needed to have addressed?

DR. WITTEN: Yes, thank you.

DR. BOYAN: Okay. Anything else?

(No response.)

DR. BOYAN: Seeing no further discussion, I am going to turn this over to Ms. Nashman, who will again inform us what the mechanics are for the voting process.

MS. NASHMAN: I know this is getting a bit tedious, having done three of these in a very short period of time; yet I still need to read the voting instructions, lest you all have forgotten.

Now that you've finished your discussion, you'll be asked to formally vote on the recommendation to the FDA on the submission. Dr. Boyan again will ask for a motion from the panel and there are three options. Those are approvable, approvable with conditions or not approvable. Again I'm just going to read through this to reinforce your memory.

They're described as follows. If you vote that the PMA is approvable, you're saying that the FDA should approve the PMA with no conditions attached. If you vote for a recommendation of approvable with conditions, you're attaching specific conditions to your recommendation that FDA approve the PMA. The conditions must be specified when a motion for approvable with conditions is made. In other

words, you may not vote for approvable with conditions and then determine the conditions later.

Examples of preapproval conditions are changes in draft labeling and resolution of questions discussed. Examples of post-approval conditions are post-market studies and the submission of periodic reports. In all cases you need to propose the extent of the conditions of approvability. This includes the number of patients to be followed and/or the number, interval and types of reports to be considered. In all cases you must state the reason or the purpose for the condition.

The third option for recommendation is that of nonapproval. The act, Section 515(b), Part 2, paragraphs A through E, state that a PMA can be denied approval for a number of reasons. The first three most relevant are a lack of showing of reasonable assurance that a device is safe under the conditions of use prescribed, recommended or suggested in the labeling. The second reason is to suggest a lack of showing of reasonable assurance that the device is effective under the conditions of use prescribed, recommended or suggested in the labeling. And the last is that you believe that the proposed labeling is false or misleading.

If you vote for disapproval, FDA asks that you identify the measures that you believe are necessary or the steps that should be taken to place the application in an approvable form.

The voting process is going to begin with a motion from a member of the panel. It may be any of the three formsÊ-- again, recommendation of approvable, approvable with conditions or nonapprovable. If the motion is seconded, the chair will ask if anyone would like to discuss the motion, and we'll continue from there.

Again, pleas e remember that the proceedings are taped for later transcription. Nonverbal signals are not captured on tape. If you wish to second, you should state so rather than nodding your head or waving your hand. And when you vote, you'll need to do so verbally, not just by a show of hands. Your vote may either be a yes, a no or an abstention.

The majority vote carries the motion and the voting members for this afternoon's portion of the meeting are as follows: Drs. Besser, Greenwald, Markolf, David Nelson, Roger Nelson, Rangaswamy, Rudicel and Skinner. Dr. Boyan, as the chairperson, votes only in the case of a tie.

At this point I will turn the voting process over to Dr. Boyan.

DR. BOYAN: Okay. First let me state that I need to entertain a motion. The motions, again, can be approvable, approvable with conditions or not approvable. Do I hear a motion?

DR. MARKOLF: I move for approval with the conditions that we have discussed.

DR. BOYAN: Okay. Do I have a second for the motion? The motion is vote for approvable with conditions, as discussed.

DR. WITTEN: Excuse me. I think it would be helpful for us if you could just enumerate those conditions as part of your motion.

DR. MARKOLF: Barbara, you've been writing them down?

DR. BOYAN: I've been writing them down, yes. The conditions, as discussed, are that the surgeon information include the discussion of the use of screws for using theÊ-- Dr. Skinner, will you do me the courtesy of doing the conditions? You state it so clearly.

DR. SKINNER: W hich conditions?

DR. BOYAN: The condition for using the acetabular cup in a freshÊsurgical situation.

DR. SKINNER: The indications, you mean?

DR. BOYAN: Yes.

DR. SKINNER: The indications would be this device is a constrained acetabular linear and is intended to be used for total hip arthroplasty in patients with a high risk of dislocation and cases such as previous multiple dislocation history, severe joint laxity, deficiency of surrounding musculature, bone loss, neuromuscular disorders and/or previous surgery.

DR. BOYAN: Okay. That was condition number one. And condition number two had to do withÊ-- David Nelson, maybe you could phrase that one for us.

DR. DAVID NELSON: That there's a relative contraindication to fresh implantation with an ingrowth cup and not using the screws. Now, that may be phrased better, but that would be it.

And I'd like the third condition to be what Dr. Skinner mentioned before, that the information of use to the surgeon that's normally contained in the package insert be placed in the surgical technique manual, where it's available to the surgeon prior to the time of surgery.

DR. BOYAN: All right. So those are the three conditions for voting for the motion. Is there a second for that motion?

DR. DAVID NELSON: I'll second.

DR. BOYAN: Dr. David Nelson seconded the motion. Is there any discussion of the motion?

(No response.)

DR. BOYAN: Hearing no discussion, then I suggest that we begin with Dr. Roger Nelson, going this way around the room, and vote to approve the motion, disapprove the motion or abstain.

DR. ROGER NELSON: Roger Nelson. Approve the motion.

DR. BOYAN: Dr. Markolf? Well, the motionÊ--

DR. ROGER NELSON: Approve the motion with conditions.

DR. BOYAN: We've already handled that. The motion has the conditions and now we're approving the motion, which contains the conditions, and then we'll go around and discuss it. So you approve the motion as it stands.

DR. ROGER NELSON: As it stands and the rationale being the discussion we've had in the past few hours.

DR. BOYAN: Right. You don't need to give us the rationale until we get the vote in.

Dr. Markolf.

DR. MARKOLF: Approval.

DR. DAVID NELSON: David Nelson, approval.

DR. BOYAN: Approval?

DR. BESSER: Mark Besser, approval.

DR. RANGASWAMY: Leeta Rangaswamy, approval.

DR. RUDICEL: Sally Rudicel, approval.

DR. GREENWALD: Seth Greenwald, approval with the conditions stated.

DR. SKINNER: Harry Skinner, approval with the conditions stated.

DR. BOYAN: All right. This means t he motion carries. Now, the motion had the conditions in it. It really and truly did.

Now, the next thing that we need to do is go around the room and discuss why you voted for approval, if you would like to make any further statements about it. And again we'll start with you, Dr. Nelson.

DR. ROGER NELSON: Roger Nelson. I approved it because of the robust scientific literature provided.

DR. BOYAN: Dr. Markolf.

DR. MARKOLF: I approved it because it was well characterized in terms of mechanical testing and it's a valid tool in the surgeon's armamentarium.

DR. DAVID NELSON: David Nelson. I approved it because, based on the FDA's definition of valid scientific evidence, I think there was such, that the device is safe

and effective, and I think that the advantages outweigh the disadvantages and that this should be an option available to some surgeons for treating certain cases.

DR. BOYAN: Dr. Besser.

DR. BESSER: I approved it because of the discussion we've had over the past few hours.

DR. BOYAN: Dr. Rangaswamy.

DR. RANGASWAMY: I approved it on the basis of everything that's been said so far.

DR. BOYAN: Dr. Rudicel.

DR. RUDICEL: I approved it on the basis of the discussion we've just had.

DR. BOYAN: Dr. Greenwald.

DR. GREENWALD: I approved it on the basis of valid scientific evidence presented and that I believe that the benefit that it affords a very limited number of patients outweighs the potential harm that derives from it, significantly.

DR. BOYAN: And Dr. Skinner.

DR. SKINNER: I approved the motion based on the presentation of valid scientific information from the FDA and from Osteonics Corporation.

DR. BOYAN: Okay. So, in summary, the recommendation of the panel is that the premarket approval

application for Osteonics Corporation's constrained acetabular be recommended for approval with conditions as we stated. And I'd like to turn the meeting back over to the executive secretary.

MS. NASHMAN: Thanks. I'll be brief and if everybody could just stay seated for one more minute. Give me two, perhaps.

I'd like to thank all the panel members at this time for their time, effort and energy in reviewing this stack of information. I'd also like to remind you that if you want the review material that you've brought with you destroyed or that we've given to you, if you'd like that information destroyed, please leave it in front of your seat and place your name card in front of it.

If you have any material in your office, please feel free to destroy it or to send it back. I've given you all mailing supplies in the blue folder I left on the table yesterday.

Also within the blue folder I left for you yesterday there is a sheet of paper which asks you to certify how you have either returned the material or destroyed the material. I need this for FDA recordkeeping.

Please also take with you any notes that you have madeÊ-- either take with you or leave here for destruction

any notes that you have made during the course of this panel meeting. If you give them to me, they will become part of the record, and I'm sure you don't want that.

Again, thank you very much for your efforts and I will see you next time, which right now is tentatively scheduled for October 15 and 16.

DR. BOYAN: And I'd like to thank everybody for being here. The meeting is adjourned.

(Whereupon, at 3:05 p.m., the committee was adjourned.)